

# Design of Multistage Counter-Current Liquid–Liquid Extraction for Small-Scale Applications

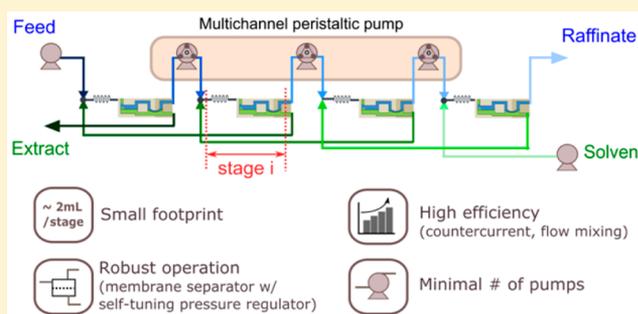
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## S Supporting Information

**ABSTRACT:** Multistage counter-current liquid–liquid extraction (MCCE) is a common unit operation in the chemical industry, but the technique is often difficult to use at laboratory and small production scales, because most MCCE systems are gravity-driven and require a large volume (~100 mL). We present a new MCCE design that integrates segmented flow mixing and membrane-based phase separators to achieve equilibrium extraction at each stage. Multichannel peristaltic pumps transfer fluids from stage to stage in a counter-current manner, rather than dedicated pumps at each stage. A self-tuning pressure control element incorporated into each separator allows robust operation, even in the presence of variation between stages and imprecise pumping. Experimental data from two classical ternary case studies (toluene–acetone–water and ethyl acetate–acetic acid–water) compare well to ASPEN Plus simulations, showing that the extraction efficiency is ~100%, regardless of the number of stages. Finally, we demonstrate the efficiency of the small-scale MCCE system (~2 mL/stage) with an industrial example of recovery of THF and ethyl acetate from methanol, ethanol, iso-butanol, and *tert*-butanol mixtures.



## 1. INTRODUCTION

Liquid–liquid extraction plays an important role in multistep chemical processing, in that it has advantages of consuming low energy (compared to distillation) and being suitable for purification of thermally sensitive compounds. In practice, multistage extraction or multiple washes is often required to achieve a high degree of separation, especially for systems with low partition coefficients or low selectivity. Multiple stages are typically cascaded into either cross-current or counter-current configurations. For a cross-current configuration, the solvent entering each stage is fresh, and the extract phase is not delivered to another stage, but combined with the extract outlets from other stages. Therefore, global flow directions of the two immiscible phases are in the same direction. On the other hand, for the counter-current configuration, the two immiscible phases are globally moving in the opposite direction. In theory, for the same solvent usage, the counter-current configuration yields the highest extraction efficiency.<sup>1</sup>

Continuous extraction at a small scale has a wide range of applications, from flow chemistry<sup>2,3</sup> to the development of extraction process. Industrially, mixer settlers and columns have been used to obtain a high number of theoretical stages,<sup>4,5</sup> but designs with small volume are rare, because of complex moving parts. So far, extraction in organic flow synthesis has been demonstrated only with a single stage<sup>6,7</sup> or cross-current

(sequential) cascading.<sup>8–10</sup> Only a few small-scale systems use multistage counter-current extraction (MCCE), which can be categorized into two types, based on arrangement of contacting units: differential and discrete (Figure 1).

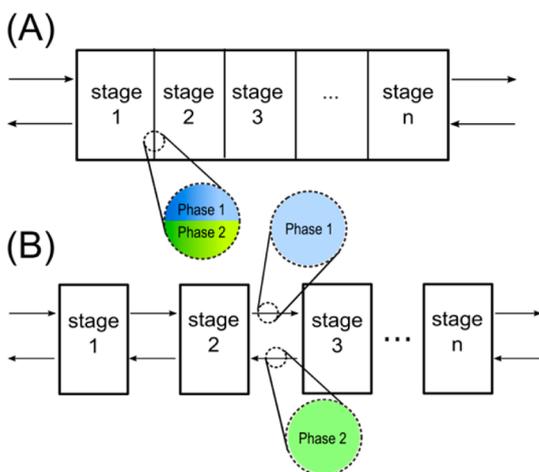
Differential contacting involves multiple stages operated continuously in a single piece of equipment, without any separation device between stages, such as rotating-disk contactors,<sup>11</sup> and Scheibel<sup>12</sup> and Karr<sup>13</sup> columns. Such columns have recently been miniaturized for laboratory-scale<sup>14,15</sup> application, but the design has limited flow space, because viscosity and surface forces dominate at small scale.<sup>16</sup> In microfluidics, Aota et al. has created counter-current flow by using selective surface modification of channel walls to maintain the interface and obtained a theoretical plate number of 4.5 for the aqueous-toluene extraction example.<sup>17</sup> Alternatively, the interface can be stabilized by a physical barrier along which the two phases flow.<sup>18</sup> However, the high shear stress at the liquid/liquid interface makes it difficult to extend this method to a very high number of theoretical stages without interfacial breakup.

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**Figure 1.** Two types of arrangement of contact units in counter-current extraction: (A) differential and (B) discrete.

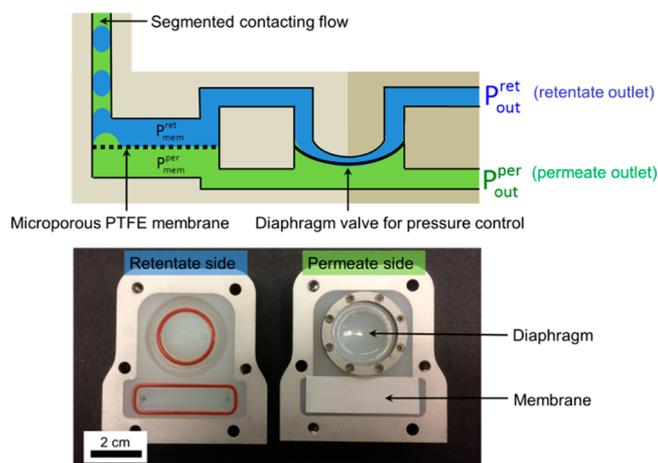
The discrete format is operated stage-wise in multiple pieces of equipment (Figure 1). This type of MCCE generally requires phase separation before pumping individual phases to adjacent stages. Examples include conventional mixer settlers and centrifugal extractors,<sup>19</sup> but these devices, even scaled down versions, still require a significant holdup volume (>100 mL) and are impractical for most laboratory-scale applications.<sup>20–23</sup> Recently, a design that implements contacting small-channel flow followed by a phase separator for each extraction stage emerged as an alternative for MCCE setup.<sup>24,25</sup> A small channel—in this context, referring to a channel with a hydraulic diameter in micrometers or submillimeters—provides a high surface-to-volume ratio, which enhances mass transfer rate.<sup>26–31</sup> In these channels, liquid–liquid flow patterns can vary from parallel to slug to irregular droplet flows.<sup>32,33</sup> We utilized the discrete slug flow regime in this paper. This regime has an enhanced mixing rate, because of internal convective circulation and large contacting surface area with a surface-to-volume ratio of 830–3200 m<sup>2</sup>/m<sup>3</sup>, which is higher than that in most large-scale conventional equipment.<sup>26,32</sup>

Following the contacting flow in each extraction stage is a phase separator. Most current laboratory-scale MCCE exploits the combined effects of surface and gravity forces,<sup>32,34</sup> but these designs require precise pumping between stages to maintain proper pressure balance. Our laboratory has developed a separation device that integrates a thin porous fluoropolymer membrane that is selectively wet by nonaqueous liquids.<sup>35,36</sup> For successful operation, a pressure drop across the membrane ( $\Delta P_{\text{mem}} = P_{\text{out}}^{\text{ret}} - P_{\text{out}}^{\text{per}}$ ) must be maintained between a capillary pressure ( $P_{\text{cap}}$ ) and a permeation pressure ( $P_{\text{per}}$ ). The latter is defined as a sufficient pressure difference to cause the wetting liquid to completely permeate through the membrane:<sup>37</sup>

$$P_{\text{cap}} > \Delta P_{\text{mem}} > P_{\text{per}} \quad (1)$$

$P_{\text{cap}}$  and  $P_{\text{per}}$  can be estimated using properties of liquids and the membrane. In our previous work, we implemented a self-tuning pressure control element (see Figure 2) to ensure that proper  $\Delta P_{\text{mem}}$  is always maintained.<sup>37</sup> This element decoupled the separator from any downstream pressure fluctuation.

The self-tuning pressure control element enabled us to construct a three-stage counter-current extraction, using three separators and two in-line HPLC pumps for interstage



**Figure 2.** Diagrams of a membrane-based separator integrated with a self-tuning pressure control element. The drawing is adapted from Adamo et al.<sup>37</sup>

pumping. The setup resulted in almost 100% extraction efficiency,<sup>37</sup> but there were challenges with the setup:

- The number of pumps required is at least  $n + 1$  for  $n$  stages, making the setup expensive.
- HPLC pumps are not self-priming; the mismatch between set and actual flow rates may cause a loss of priming and, eventually, pump failure.

Herein, we investigate operating regimes of the separator in the presence of interstage pumping with inexpensive multi-channel peristaltic pumps. We use peristaltic pumps to accommodate the changing flow rates that result from the extraction. The present systematic study shows that it is possible to achieve complete separation even when the interstage pumping rate does not perfectly match with its actual retentate outlet flow rate. We demonstrate the MCCE setup with peristaltic pumps with ternary and multicomponent case studies. We anticipate this MCCE setup will serve as a multipurpose platform. Our recent study demonstrated that this setup can be integrated to continuous-flow synthesis to achieve high purity with minimal solvent consumption.<sup>38</sup> In addition, it could be used in the development of an extraction process to screen several process variables before pilot-plant testing, as well as to validate simulation results.

## 2. OPERATING PRINCIPLE

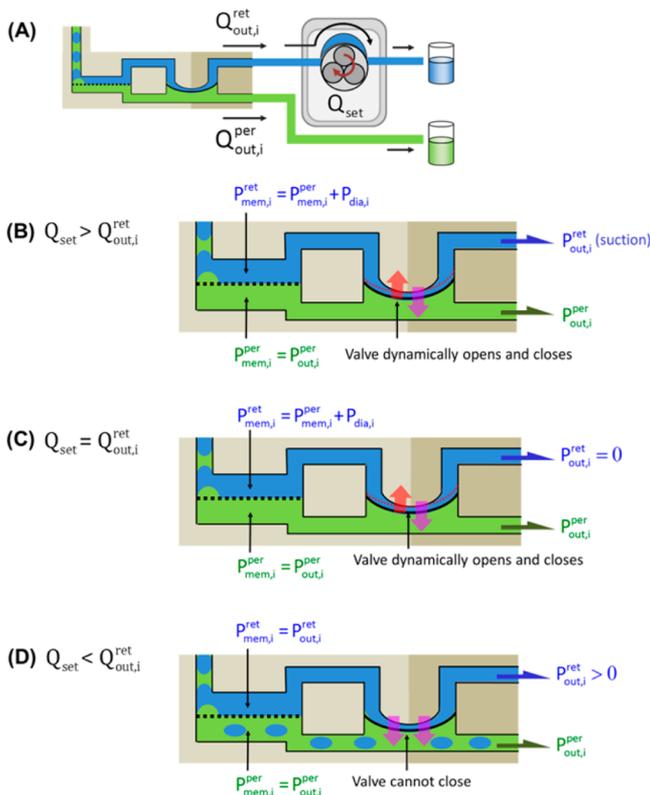
The membrane separator incorporates a pressure control element that is made of an elastic, resilient diaphragm that can seal against and provide an additional force ( $P_{\text{dia}}$ ) on the retentate flow path. Therefore,  $P_{\text{mem}}^{\text{ret}} = P_{\text{mem}}^{\text{per}} + P_{\text{dia}}$ , and the expression given in eq 1 becomes

$$P_{\text{cap}} > P_{\text{dia}} > P_{\text{per}} \quad (2)$$

The expression in eq 2 suggests that we no longer need to regulate the pressures of the two outlets ( $P_{\text{out}}^{\text{ret}}$  and  $P_{\text{out}}^{\text{per}}$ ) independently for each individual unit. Instead,  $\Delta P_{\text{mem}}$  self-tunes to a fixed pressure difference  $P_{\text{dia}}$  that has a value within the operating window for complete phase separation. Thus, given the proper design and material of the diaphragm, the phase separation will be successful and isolated from the downstream pressure disturbance.

The pressure control element simplifies the implementation of the separators into a cascading system. Before constructing

the multistage cascade, we examine how interstage pumping could affect the separator's performance in three possible scenarios for retentate outlet manipulation (see Figure 3). Note that the subscript  $i$  refers to the stage number.



**Figure 3.** (A) Schematic of the separation unit operation with peristaltic pumping at the retentate outlet. Also shown is an investigation of three possible scenarios of interstage pumping: (B)  $Q_{set} > Q_{out,i}^{ret}$  (C)  $Q_{set} = Q_{out,i}^{ret}$  and (D)  $Q_{set} < Q_{out,i}^{ret}$ . Note that the red and purple arrows indicate dynamic movement of the diaphragm.

When the separator operates as a standalone without any pumping at the retentate outlet,  $P_{mem,i}^{ret}$  will be automatically tuned to  $P_{mem,i}^{per} + P_{dia,i}$ . This also happens when the retentate flow rate ( $Q_{out,i}^{ret}$ ) matches perfectly with the downstream pumping rate ( $Q_{set}$ ) (see Figure 3C). When  $Q_{set} > Q_{out,i}^{ret}$ , the separation still works because  $P_{mem,i}^{per}$  is sufficient to force the diaphragm to close the retentate flow path and provide a tuning pressure for  $P_{mem,i}^{ret}$  (see Figure 3B). On the other hand, when  $Q_{set} < Q_{out,i}^{ret}$ , the pump becomes a partial blockage for the retentate outlet.  $P_{out,i}^{ret}$  increases sufficiently to open the diaphragm valve (Figure 3D), resulting in a lack of proper pressure tuning and incomplete separation. Therefore, it is possible to implement interstage pumping, even with non-precise pumps, as long as we specify  $Q_{set} \geq Q_{out,i}^{ret}$ .

We chose to use peristaltic pumping for several reasons. First, unlike other positive displacement pumps, it allows for slippage. Therefore, the peristaltic pump is less prone to mechanical damage, in the event of a mismatch between the set  $Q_{set}$  and  $Q_{out,i}^{ret}$ , particularly when operating in excess of the extent of suction. Second, each peristaltic pump can accommodate multiple channels on the same roller drive. Pumping multiple lines on a single pump reduces cost or footprint of the overall setup. While the peristaltic pump can be nonprecise, this MCCE setup overcomes this disadvantage

because the pumping rate ( $Q_{set}$ ) does not need to be accurate. Provided that  $Q_{set}$  is set to be equal to or higher than  $Q_{out,i}^{ret}$ , the separation will be successful, regardless of how much  $Q_{set}$  deviates from the actual  $Q_{out,i}^{ret}$ .

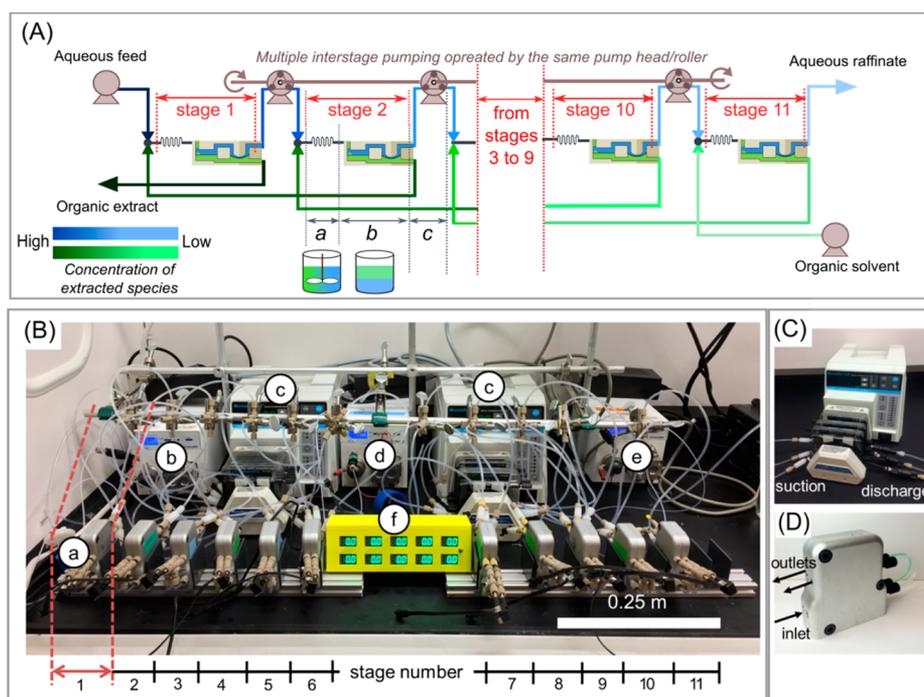
### 3. EXPERIMENTAL SECTION

**3.1. Membrane-Based Separator.** The membrane separator was modified from the original design in polycarbonate.<sup>37</sup> To ensure chemical compatibility, the wetted structure was machined in ultra-high-molecular-weight polyethylene (UHMWPE), which is compatible with most organic solvents. The outer shell was made of aluminum for enhanced mechanical properties. The filters used were 0.5- $\mu\text{m}$ -pore polytetrafluoroethylene (PTFE) membranes (Pall Corporation) and 0.1- $\mu\text{m}$ -pore PTFE laminated membranes (Sterlitech). The choice of the filters was dependent on the interfacial tension. The 0.1- $\mu\text{m}$ -pore diameter membrane is more suitable for low interfacial tension systems. The diaphragm was made of a perfluoroalkoxy (PFA) film.

**3.2. Multistage Counter-Current Extraction Setup.** The pumps used for interstage pumping were Masterflex L/S 8-channel, three-roller peristaltic pumps (Cole-Parmer, USA), which each could accept up to eight flow paths for synchronous flow. The cartridges could be snapped in and out for quick and simple tubing changes. The peristaltic tubing used was Gore Style 500, Gore Style 100, Norprene A-60-G tubing with L/S 14 size. They were used in different tests according to their different chemical resistances.

Figure 4 shows the arrangement of the extraction stages. All tubing was PFA with  $1/8$ -in. OD and  $1/16$ -in. ID (McMaster-Carr, USA). The two phases were mixed in a T-mixer (IDEX, USA). The tubing was cut to a length that allowed more than 10 s in residence time to ensure equilibrium mass transfer based on typical mass-transfer coefficients for slug flow ( $\sim 0.5 \text{ s}^{-1}$ )<sup>26,39</sup> and a first-order exponential approach to equilibrium. Results below which compare observed and predicted performance, show that the system achieves  $\sim 100\%$  extraction efficiency per stage, indicating that sufficient time was allowed for complete mass transfer. Considering all tubing and the membrane separator, the total volume was  $\sim 2 \text{ mL}$  per each stage. The stage number was counted from low pressure to high pressure. The retentate outlet of stage  $i$  flowed to stage  $i + 1$  through the peristaltic pumping. The permeate outlet of stage  $i$  flowed to stage  $i - 1$  as driven by the pressure drop (no external pumping). The start-up procedure was as follows; only the membrane-wetting solvent (i.e., organic solvent) first flowed through the setup, generally from the  $N$ th stage to the first stage. If the permeate flow path of the separator was not filled with liquid, the diaphragm PFA film could inflate excessively in the presence of the retentate liquid, resulting in possible damage to the film. Once all the separators were filled with organic solvent, the pump for the nonwetting liquid (i.e., water) and the peristaltic pump were started simultaneously.

**3.3. Validation of Operating Principles.** To validate our operating principles, the separator was tested with different values of  $Q_{set}$  relative to  $Q_{out,i}^{ret}$ . Toluene and water were each flowed at 5 mL/min, combined in a T-mixer, and fed to the membrane separator. The retentate outlet was connected to the peristaltic pump with the rate  $Q_{set}$  while the permeate outlet is delivered directly to a collection vial. The flow rate through the permeate outlet was normalized by the inlet toluene flow rate (5 mL/min). This pair of solvents is almost completely immiscible. For complete phase separation,  $Q_{out,i}^{ret}$  should be 5



**Figure 4.** (A) Scheme for the 11-stage countercurrent extraction. Each stage features (a) contacting tubing, (b) separator, and (c) interstage pumping. (B) Image of the 11-stage countercurrent extraction, with total footprint dimensions of 1.0 m  $\times$  0.6 m  $\times$  0.2 m, including (a) membrane separators, (b) HPLC pump for water to the first stage, (c) peristaltic pumps for interstage delivery, (d) HPLC pump for feed to the middle stage, (e) HPLC pump for organic solvent to the  $N$ th stage, and (f) online diaphragm pressure monitoring. (C) Photograph showing the multichannel peristaltic pump. (D) Photograph showing the membrane separator.

mL/min, and the normalized permeate value should be 1.  $Q_{\text{set}}$  was varied to be higher than, equal to, and lower than 5 mL/min.  $P_{\text{out},i}^{\text{ret}}$  was also measured for each membrane unit.

**3.4. In-Line Measurement of  $\Delta P_{\text{mem},i}$  in the MCCE Setup.** The separators were then assembled into a 10-stage setup. Each separator was installed with a board mount pressure sensor (Honeywell, USA) to measure the pressure difference between the two sides of the membrane ( $\Delta P_{\text{mem},i}$ ). This experiment was to observe time-dependent stability of  $\Delta P_{\text{mem},i}$  in the scenario, for which we set the interstage pumping rate ( $Q_{\text{set}}$ ) to be higher than the wetting-phase flow rate. Water and toluene were each fed at 2 mL/min into the setup at the first and 10th stages, respectively.  $Q_{\text{set}}$  was set at 2.5 mL/min. The setup was operated for 2 h, and the reading values of  $\Delta P_{\text{mem},i}$  were recorded at different time points.

**3.5. Extraction Efficiency Experiments.** Two classical ternary systems were selected for testing the extraction efficiency of the setup. The first system was the extraction of acetone between toluene and water. This is a standardized system recommended by the European Federation of Chemical Engineers (EFCE).<sup>40</sup> In this study, a high fraction of the extracted species (acetone) was added to demonstrate the system's capability of handling variation of flow rates across stages. Also, acetone reduces the interfacial tension significantly, which makes it a challenging case study. The other system was the extraction of acetic acid between water and ethyl acetate,<sup>41</sup> which is another low-interfacial tension system. The testing conditions are given in Table 1. The measured interfacial tensions and contact angles are reported in the Supporting Information (SI). The percent extraction and efficiency were determined for each system at stages  $N = 1, 3, 5,$  and  $7$ .

**3.6. Multicomponent Solvent Recovery Case Study.** A multicomponent solvent recovery was tested as an example of

**Table 1. Experimental Conditions for Two Ternary Test Systems**

	toluene–acetone–water	ethyl acetate–acetic acid–water
feed at stage 1	0.50 mass fraction of acetone in water, 2.0 mL/min	0.05 mass fraction of acetic acid in water, 0.5 mL/min
feed at stage $N$	toluene, 1.0 mL/min	ethyl acetate, 2.0 mL/min
peristaltic pump rate, $Q_{\text{set}}$	2.5 mL/min	0.7 mL/min
characterization	gas chromatography, FID	titration

industrial relevance. The feed solvent stream contained tetrahydrofuran (THF), ethyl acetate, methanol, ethanol, isopropanol (IPA), *tert*-butanol, and trace water. The objective was to separate THF and ethyl acetate from the other components. Decane and water were effective extraction solvents. Table 2 shows the compositions in the feed stream and their partition coefficients ( $K_D$ ), measured with a feed:water:decane ratio of 1:1:1.

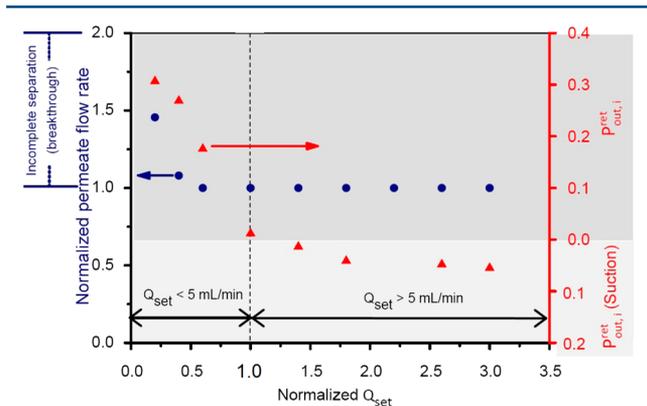
Methanol and ethanol can be separated effectively by one stage, because of their high partition coefficients. The other components require multiple stages of extraction to obtain high separation. The system was tested for  $N = 1, 3, 5, 7,$  and  $9$ . The feed, decane, and water were delivered to the system by HPLC pumps (Knauer, Germany), and they entered at the middle stage, the  $N$ th stage, and the first stage, respectively. For the purpose of demonstration, their flow rates were set at 2, 3, and 4 mL/min, respectively. The two outlets were collected at different time points and characterized using a headspace gas chromatography (HS-GC) method reported in the literature.<sup>42</sup>

**Table 2.** Feed Composition for the Multicomponent Extraction Example and the Experimental Values of  $K_D$  for Each Component

	mass fraction	$K_D$
THF	0.384	0.5
ethyl acetate	0.339	0.2
methanol	0.085	19.7
ethanol	0.005	5.6
IPA	0.045	2.6
<i>tert</i> -butanol	0.045	1.6
water	0.096	

## 4. RESULTS AND DISCUSSION

**4.1. Validation of Operating Principles.** We start by examining the principles underlying how the membrane separation performs in the presence of interstage pumping. When the normalized  $Q_{set}$  is  $<1$ , the separation is incomplete (see Figure 5). As the normalized  $Q_{set}$  becomes smaller, water

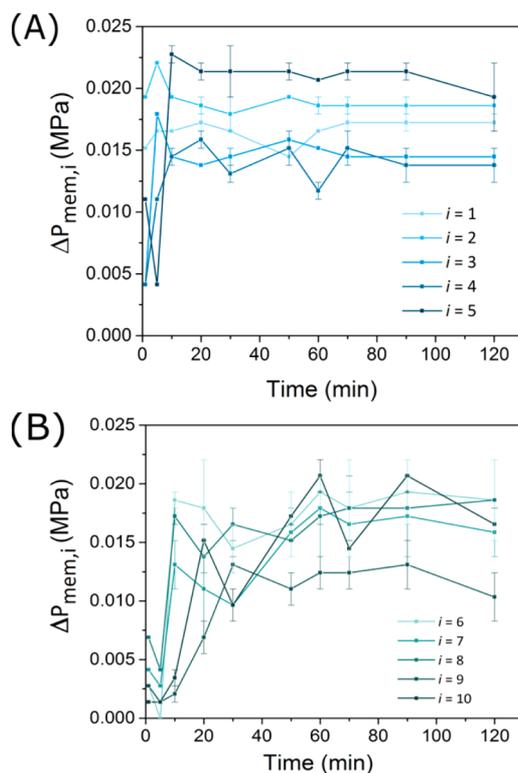


**Figure 5.** Separator's performance, as indicated by the normalized permeate flow rate, and measured values of  $P_{out,i}^{ret}$  at varied pumping rates  $Q_{set}$ , normalized by the inlet water flow rate. Toluene and water flows are 5 mL/min each. The values of  $P_{out,i}^{ret}$  are reported in units of MPa.

increasingly breaks through into the permeate outlet. This validates the principle that, when  $Q_{set} < Q_{out,i}^{ret}$  the pump serves as a partial blockage for water to exit through the retentate outlet. The blockage also generated the pressure buildup of  $P_{out,i}^{ret}$ . When  $P_{out,i}^{ret} \gg P_{out,i}^{per}$  the diaphragm is deformed downward and incapable of resiliently sealing against the retentate flow path. It can no longer govern  $\Delta P_{mem,i}$ .

On the other hand, when the normalized  $Q_{set}$  is  $\geq 1$ , we observed complete separation. In these two scenarios, the retained phase can fully flow out of the separator. An increasing value of  $Q_{set}$  can create suction, which nevertheless does not affect the separator's performance. Under normal ( $P_{out,i}^{ret} \approx 0$ ) and suction conditions, the diaphragm can deform or return to its original position without restrictions, and thereby provides the tuning for  $\Delta P_{mem,i}$ .

**4.2. In-Line Measurement of  $\Delta P_{mem,i}$  in the MCEE Setup.** In this experiment, the pressure difference between the two sides of the membrane at the  $i$ th stage ( $\Delta P_{mem,i}$ ) is measured using in-line pressure sensors (Figure 6). The fluctuations of  $\Delta P_{mem,i}$  are within error bars of 3.5 kPa. During the first 20 min, we observed a gradual increase of  $\Delta P_{mem,i}$ , which was more prominent in stages  $i > 5$ . This increase is a result of the start-up procedure described in the Experimental

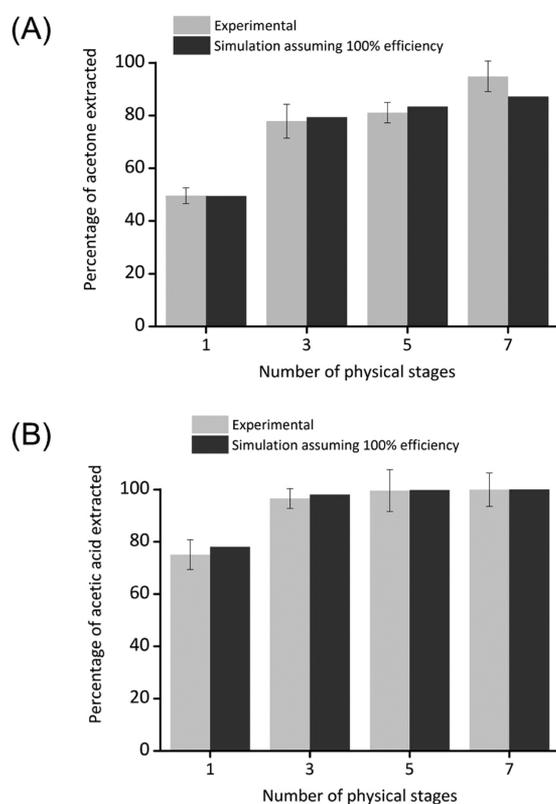


**Figure 6.** Experimentally measured values of  $\Delta P_{mem,i}$  at the  $i$ th stage in the setup with  $N = 10$ . Data are divided into two plots for clarity: (A) stages 1–5 and (B) stages 6–10.

**Section.** Toluene first flowed through the system from the 10th stage to the first stage as the membrane-wetting phase. When all the separators were filled with the solvent, the nonwetting phase (i.e., water) was pumped into the setup at the first stage. The pressure in the stages increases as water reaches the later stages. Overall,  $\Delta P_{mem,i}$  is maintained within a narrow range, between 10.3 kPa and 24.1 kPa.

**4.3. Extraction Efficiency Experiments.** High extraction efficiency can be achieved by a combination of complete solute transfer and phase separation. The solute transfer goes to completion as it approaches thermodynamic equilibrium. The performance of the setup can be evaluated by comparing the experimental percent of extraction against the equilibrium percent of extraction. The two examples of the ternary systems—toluene–acetone–water and ethyl acetate–acetic acid–water—can be accurately handled by thermodynamic models, since their interaction parameters are well-defined in the literature.<sup>43,44</sup> We incorporated those reported parameter values into ASPEN Plus simulation to calculate the percent extraction with equilibrium stages, and then compared those simulation results to the experimental results at different numbers of stages,  $N$  (see Figure 7). The experimental and simulation results closely agree, demonstrating that extraction efficiency is nearly 100% regardless of number of stages. This finding is consistent with the operating principle of our setup in which mixing and separation are arranged in discrete units. The equilibrium stage is reached given sufficiently long mass transfer in the mixing tubing and successful operation of the separator.

In order to further highlight another key feature of the setup, the ASPEN Plus simulation was employed to generate flow profiles, i.e.,  $Q_{out,i}^{ret}$  from  $i = 1$  to  $i = N$ . The simulation was performed under the conditions listed in Table 1 and  $N = 7$ . In

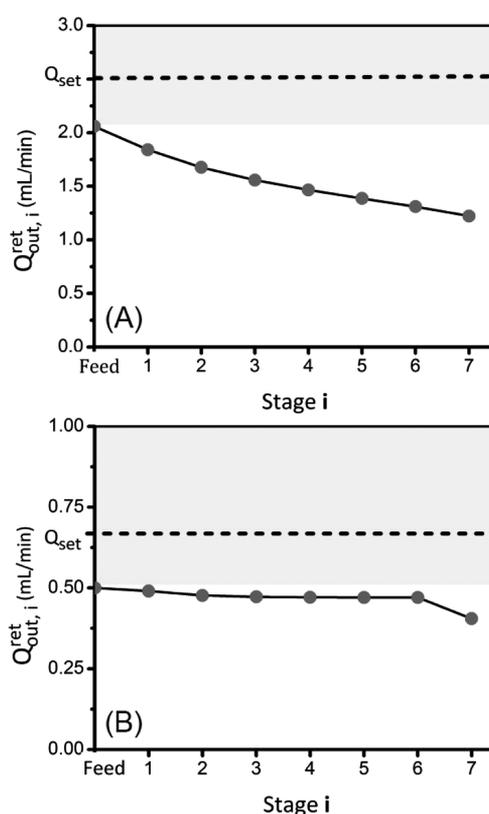


**Figure 7.** Experimental percent extractions at different numbers of stages ( $N$ ) are compared against the simulation results based on equilibrium extraction, i.e., 100% efficiency, for the two ternary examples: (A) toluene-acetone-water and (B) ethyl acetate-acetic acid-water.

other types of extraction equipment, the flow profiles must be determined beforehand, in order to accurately specify the interstage pumping rate and avoid problems such as overflow. As shown in Figure 8, the flow rates change significantly from one stage to another. The change in flow rates is more prominent in the toluene-acetone-water example, because of the large amount of extracted species (acetone). In both examples, our setup proves to be capable of handling such variation between stages. Throughout these experiments, the separators at all stages provided complete phase separation. We set  $Q_{\text{set}}$  to be higher than the inlet aqueous flow rate; therefore, the diaphragm was able to properly tune  $\Delta P_{\text{mem},i}$ . Also, the peristaltic pump offers some flexibility in relative flow rates among the different flow paths in the multichannel pump head. For other positive displacement pumps, the mismatch between  $Q_{\text{set}}$  and  $Q_{\text{out},i}^{\text{ret}}$  may result in the separator's failure or cavitation, which could potentially cause the pump to halt.

#### 4.4. Multicomponent Solvent Recovery Case Study.

The recovery of THF and ethyl acetate from a mixture of alcohols was chosen as a case study. This industrially relevant example poses many challenges in extraction process development. Although the use of computer simulations for process development is becoming increasingly important,<sup>45</sup> most thermodynamic models, even the semiempirical ones, fail to predict multicomponent liquid-liquid equilibrium. Therefore, flow profiles and effects of process variables often cannot be determined accurately prior to flowsheet design. Flow properties, such as viscosity and interfacial tension, have a tendency to vary greatly from one stage to another, because of the transfers



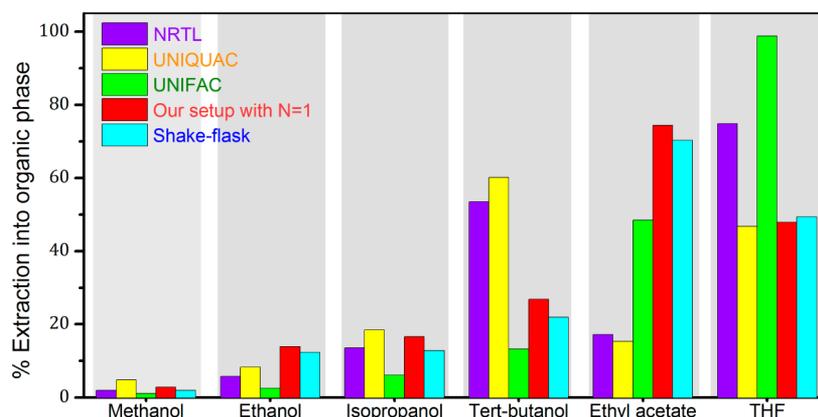
**Figure 8.** Simulated profiles of the flow rates  $Q_{\text{out},i}^{\text{ret}}$  across the seven-stage setup for the two ternary examples: (A) toluene-acetone-water and (B) ethyl acetate-acetic acid-water. The shaded areas are operating windows for  $Q_{\text{set}}$  and the dotted lines indicate  $Q_{\text{set}}$  used in our experiments.

of multiple species. When  $N > 3$ , batchwise experimental screening can be particularly tedious,<sup>46</sup> while the studies using conventional extractors are difficult to scalable, because of their complex hydrodynamics.<sup>45</sup>

The percent extraction in our setup with  $N = 1$  is compared against results obtained with the “shake-flask” method, which allows very long mixing and phase separation (>24 h in total) and, therefore, it serves as a benchmark for equilibrium extraction. The results from our setup and the shake-flask agree closely (Figure 9), indicating that each physical stage in our setup represents one equilibrium stage. On the other hand, the selected thermodynamic models (NRTL, UNIQUAC, UNIFAC) are not able to fully capture the liquid-liquid phase behavior of this system.

The setup enables screening of different extraction conditions. Since extraction in a single stage provides equilibrium, the same tubing length was used for the multistage ( $N > 1$ ) scale. The interstage peristaltic pumping rate ( $Q_{\text{set}}$ ) was set to be 6 mL/min. This is the maximum value of  $Q_{\text{out},i}^{\text{ret}}$  at any stage  $i$ , since it is based on an unlikely assumption that the entire feed is partitioned into the aqueous phase. In other words, the rate  $Q_{\text{set}}$  will be higher than  $Q_{\text{out},i}^{\text{ret}}$  at all stages, and the successful operation of the separator will be maintained. We investigate experimentally how the number of stages ( $N$ ) affects the percent recovery of THF and ethyl acetate in the organic outlet and percent removal of alcohols in the aqueous outlet.

Complete separation at all stages was achieved. Occasionally, pulsation of the peristaltic pumping propagated to the separator, causing either minor retention of the organic phase



**Figure 9.** Experimental results generated from our setup closely agree with the “shake-flask” method, while thermodynamic models fail to predict this multicomponent solvent recovery ( $N = 1$ , water:feed:decane = 1:1:1, in terms of volumetric amount).

with the retentate outlet or minor breakthrough of the aqueous phase into the permeate outlet. We are currently exploring different types of flexible interstage pumping with less pulsation.

The degree of separation increased with (i) increasing number of stages ( $N$ ), (ii) lower fraction of the alcohols in the organic outlet, and (iii) higher recovery of THF and ethyl acetate (see Figure 10). With nine stages, more than 95% of the alcohols were removed from the desired organic outlet, while the amounts of THF and ethyl acetate in the aqueous outlet were minimized. Higher recovery and purity of the THF and ethyl acetate stream could likely be obtained by simply adding

more stages or altering flow conditions, such as the solvent-to-feed ratio. Further optimization of this extraction example is beyond the scope of this contribution, but proof-of-concept examples have shown potential for facilitating the development of the multicomponent process.

## 5. CONCLUSIONS

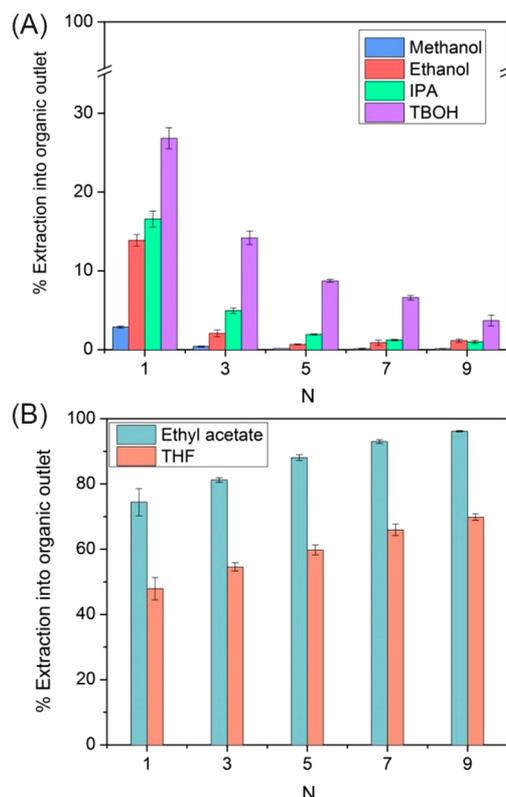
The new low-volume multistage counter-current liquid–liquid extraction (MCCE) design integrates segmented flow mixing and membrane-based phase separators to achieve equilibrium extraction at each stage. To reduce the cost of pumps and allow for the changing mass flows of the extracted stream, multichannel peristaltic pumps transfer fluids from stage to stage in a counter-current manner. The self-tuning pressure control element incorporated into each separator enabled robust operation, even in the presence of variation between stages and imprecise pumping, as long as the pumping rate was equal to or higher than the actual flow rate of the separator’s effluent on the retentate side. Experimental data from two ternary case studies—toluene–acetone–water and ethyl acetate–acetic acid–water—compared well to ASPEN Plus simulations, revealing that the extraction efficiency was  $\sim 100\%$ , regardless of the number of stages, because of the high mass transfer in slug flow preceding the separator. An industrial case study demonstrated the efficiency of the small-scale MCCE system ( $\sim 2$  mL/stage) with extraction of THF and ethyl acetate from methanol, ethanol, iso-butanol, and *tert*-butanol mixtures. The results from this multicomponent system closely agreed with batch equilibrium extraction, highlighting the potential of the setup for generating equilibrium data for the development of extraction processes.

## ■ ASSOCIATED CONTENT

### 📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.iecr.7b00434.

Complete details about the parameter used in ASPEN Plus simulation for the two ternary systems, the multistage extraction setup, the headspace-GC method for the multicomponent solvent recovery system (PDF)



**Figure 10.** Percent extractions of all components into the organic outlet for the multicomponent solvent recovery with different number of stages ( $N$ ) and a feed:decane:water ratio of 2:3:4. Data are divided into two plots for clarity: (A) alcohols, and (B) THF and ethyl acetate.

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### Notes

The authors declare no competing financial interest.

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## NOTATION

### Abbreviations

HPLC = high-performance liquid chromatography  
 MCCE = multistage counter-current liquid–liquid extraction  
 PTFE = polytetrafluoroethylene  
 UHMWPE = ultrahigh-molecular-weight polyethylene

### Variables

$N$  = total number of stages in the setup  
 $P_{\text{mem}}^{\text{ret}}$  = pressure of liquid on retentate side of membrane  
 $P_{\text{mem}}^{\text{per}}$  = pressure of liquid on permeate side of membrane  
 $P_{\text{dia}}$  = pressure exerted by resilient diaphragm  
 $P_{\text{cap}}$  = capillary pressure between two immiscible phases inside membrane pores  
 $P_{\text{per}}$  = permeation pressure (pressure drop required for the wetting liquid to permeate through the membrane)  
 $P_{\text{out}}^{\text{ret}}$  = pressure of retentate liquid at the outlet of the separator  
 $P_{\text{out}}^{\text{per}}$  = pressure of permeate liquid at the outlet of the separator  
 $Q_{\text{out}}^{\text{ret}}$  = volumetric flow rate of retentate liquid at the outlet of the separator  
 $Q_{\text{out}}^{\text{per}}$  = volumetric flow rate of permeate liquid at the outlet of the separator  
 $Q_{\text{set}}$  = pumping rate set on the peristaltic pump  
 $K_{\text{D}}$  = partition coefficient, defined as concentration (mg/mL) in aqueous phase over concentration (mg/mL) in organic phase

### Subscript

$i$  = stage number

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