Supporting Information for

Improved Slit-shaped Microseparator and its Integration with a Microreactor for Modular Biomanufacturing

Souryadeep Bhattacharyya,[1,2] Pierre Desir, [1,2] Sebastian Prodinger[1,2], Raul F. Lobo[1,2] and Dionisios G. Vlachos[1,2*]

[1]Department of Chemical & Biomolecular Engineering, University of Delaware, 150 Academy St., Newark, DE 19716, USA
[2]Catalysis Center for Energy Innovation, RAPID Manufacturing Institute, and Delaware Energy Institute (DEI), University of Delaware, 221 Academy St., Newark, DE 19716, USA

* Corresponding author: vlachos@udel.edu

1

The hydraulic pressure drop in **Figure 2B** was estimated using the Hagen–Poiseuille equation:

$$\Delta P_{hyd} = \frac{12\mu FL}{WH^3}$$

(S1)

where μ is the dynamic viscosity (Pa-s), F is the flow rate (m³/s), L, W and H are the length, width and height of the slit (m) respectively.

The capillary pressure in **Figure 2B** was estimated using the Young–Laplace equation:

$$\Delta P_{cap} = \gamma\left(\frac{2}{H} + \frac{2}{W}\right)$$

(S2)

where γ is the interfacial tension (N/m)

The slit height is a design variable and a 1.5 mm slit height was used in this work. The slit length and width were 5 and 10 mm, respectively.

2

Supporting Figures
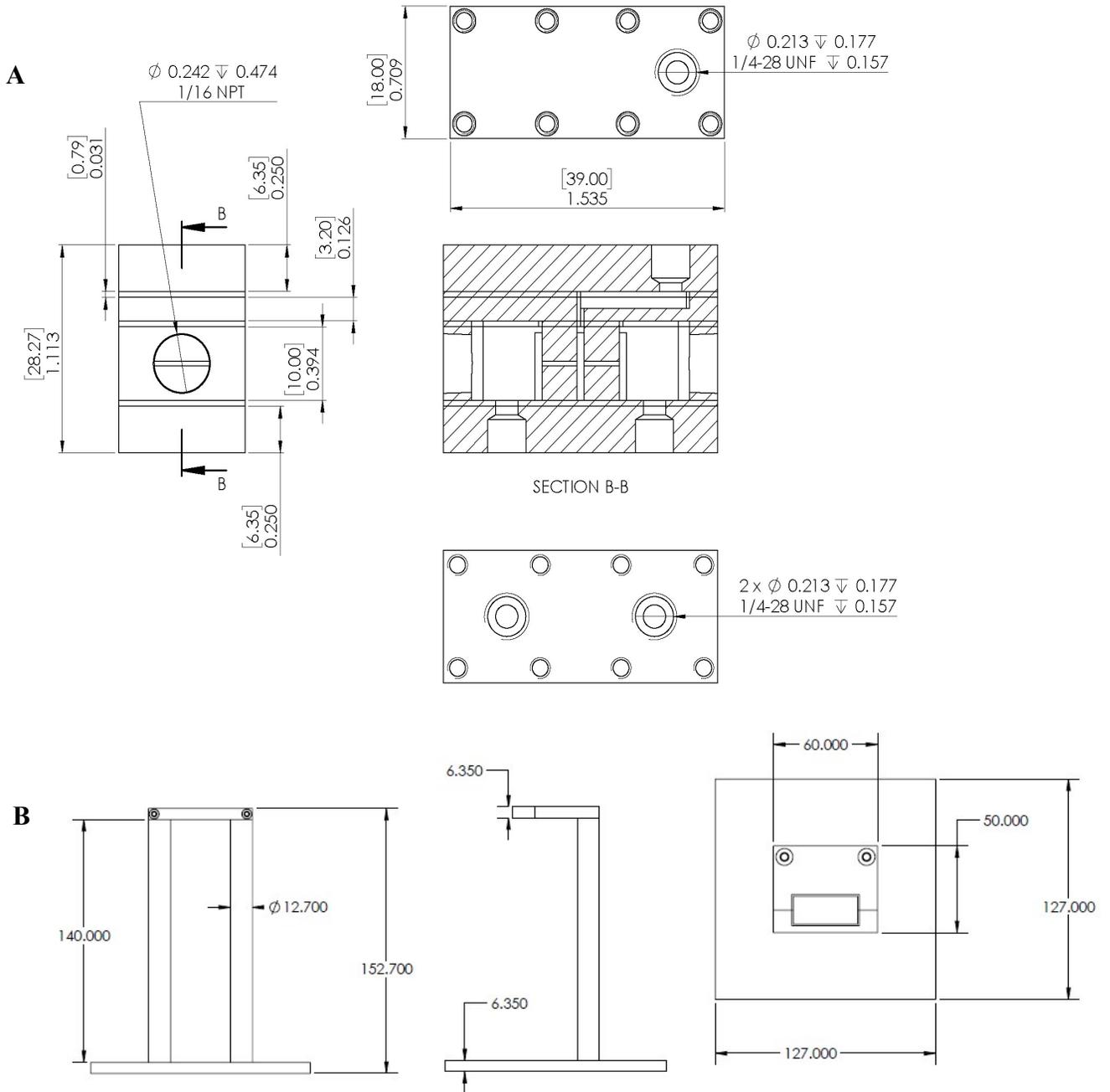
Figure S1. Design dimensions of **A)** the slit-separator with its different components and **B)** holding rig for the microseparator.

3
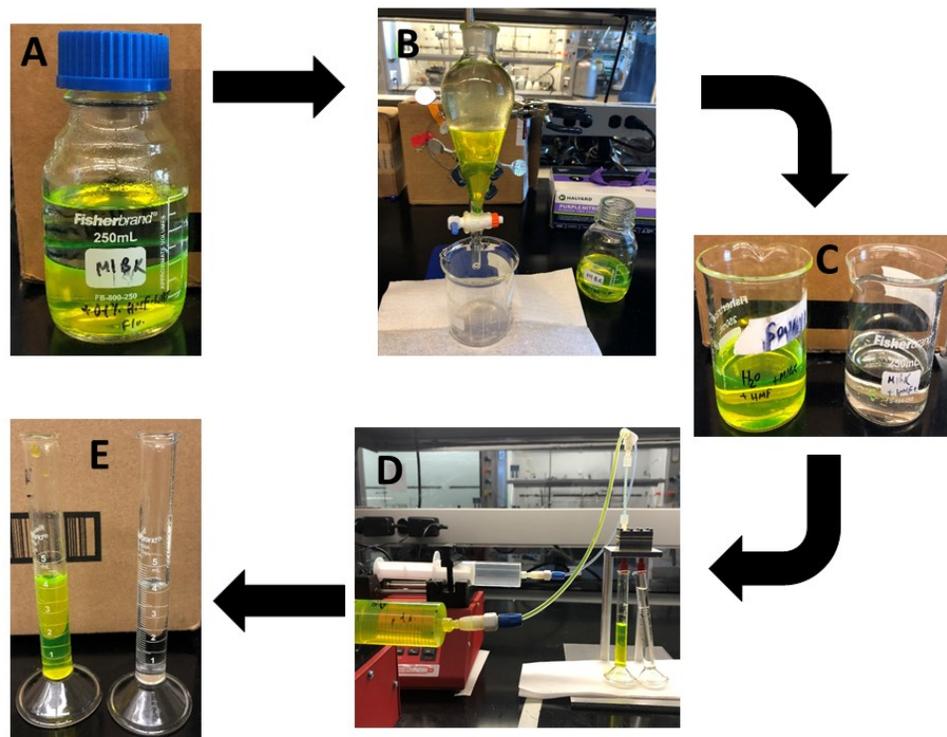
Figure S2. Experimental scheme for evaluation of microseparator performance in biphasic systems: A) pre-equilibration, B, C) phase separation using a separatory funnel, D) pumping of the two pre-equilibrated phases into the microseparator with syringe pumps via a tee-junction outlet, and E) liquid samples collected at the separator outlet for visual inspection and quantification using HPLC and KF titration. The initial aqueous phase contains 0.1 wt. % HMF and 0.3 g/L fluorescein (for visualization).
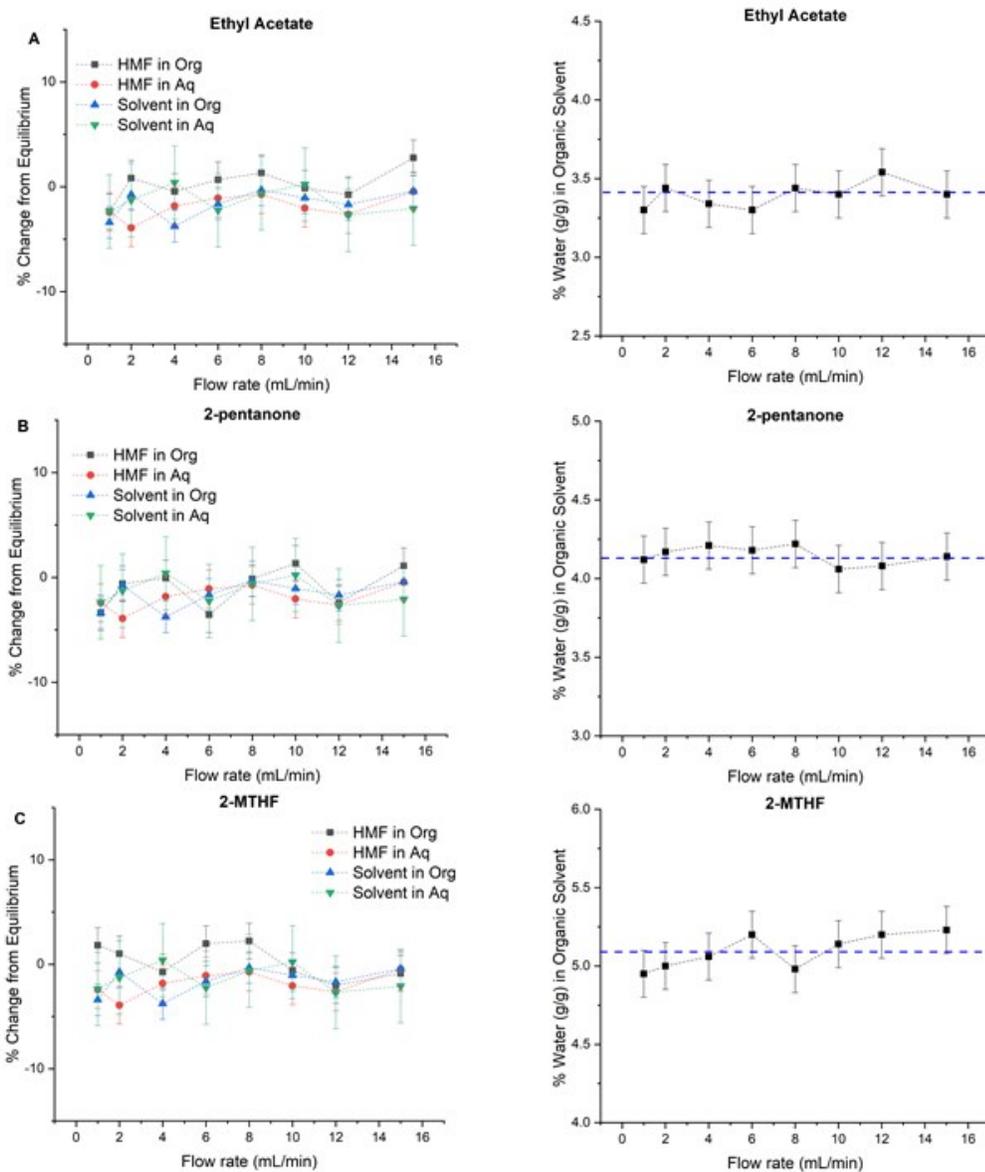
Figure S3. HPLC quantification of HMF and solvent concentration deviation at the microseparator outlets from the pre-equilibrated inlet phases for A) ethyl acetate, B) 2-pentanone, and C) 2-MTHF with the corresponding organic phase water content (KF) across a 1-15 mL/min flowrate range with 1:1 flow ratio. Dotted blue lines indicate equilibrium water content in the organic phase. Errors bars indicate total sampling and instrumental error.
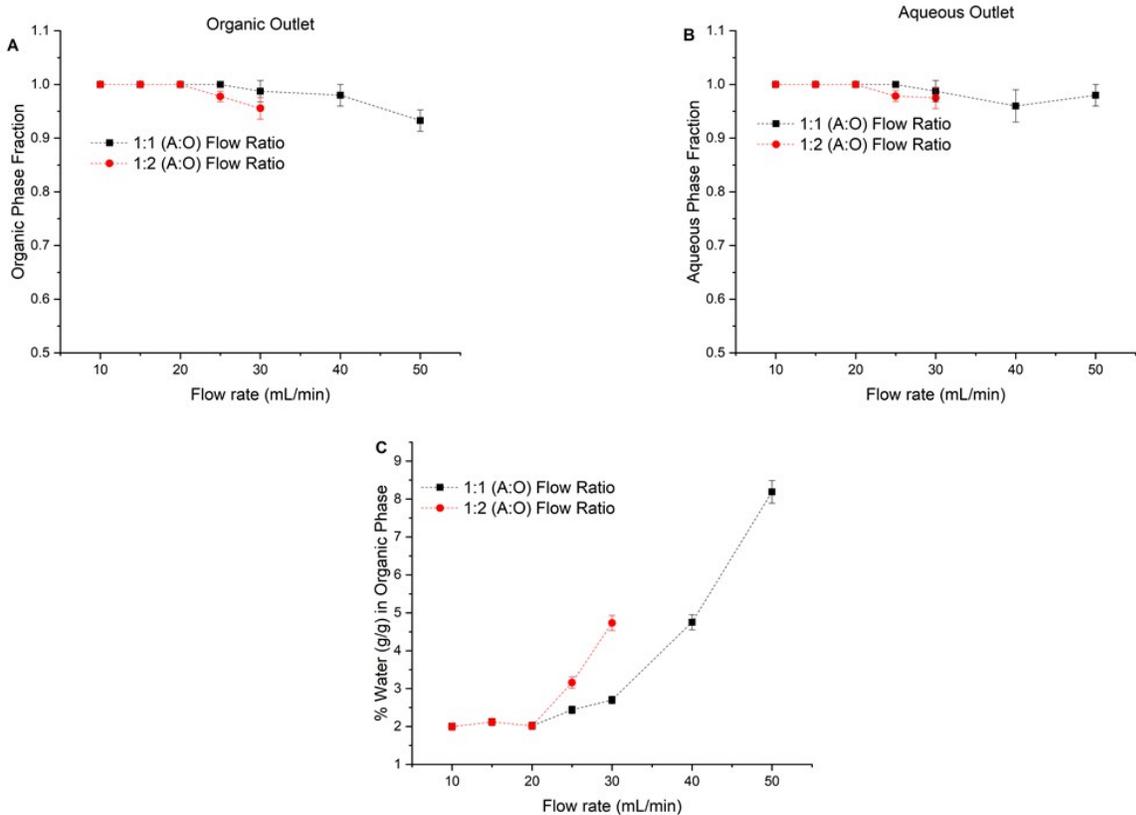
Figure S4. Microseparator performance at **A)** organic outlet, **B)** aqueous outlet, and **C)** corresponding organic phase water content (KF) with an increasing flow rate of the MIBK/water biphasic system at 1:1 and 1:2 A:O phase flow ratios.
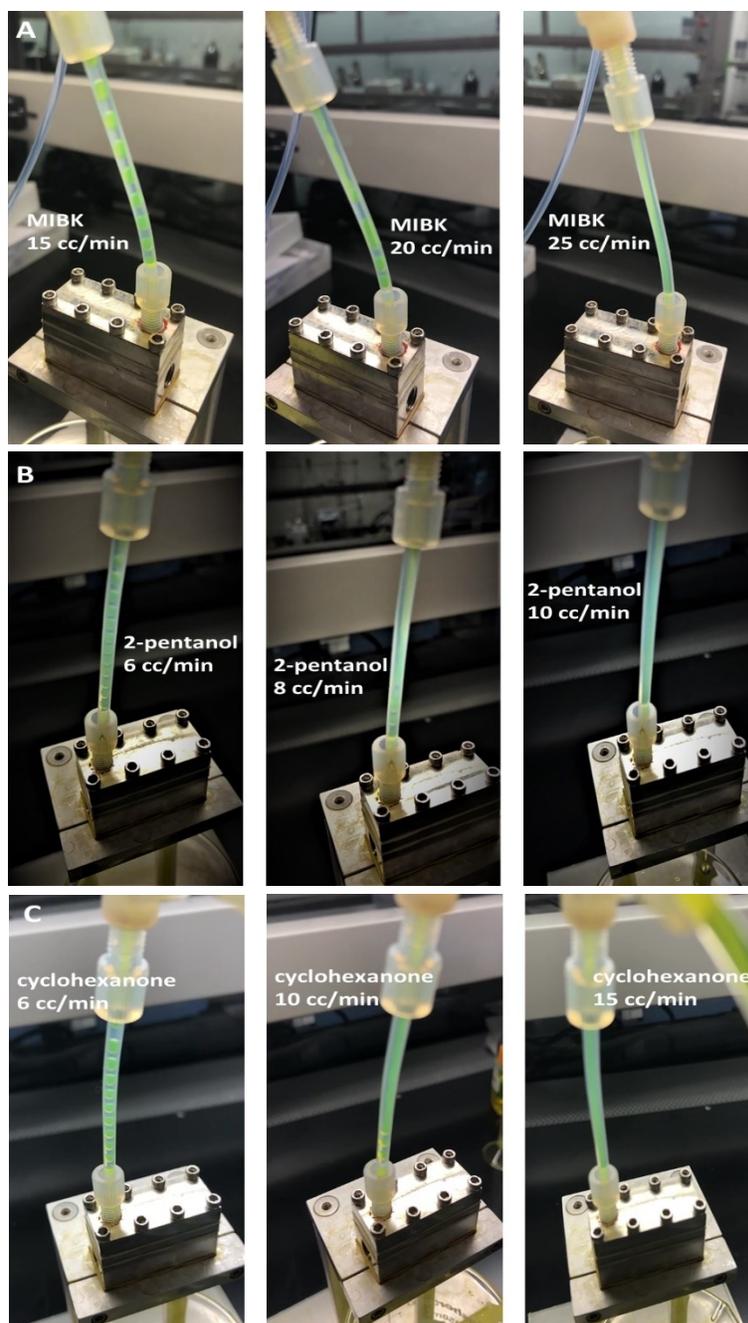
Figure S5. Transitions from segmented (L), transitional (M) to non-segmented (R) flow for **A)** MIBK, **B)** 2-pentanol, and **C)** cyclohexanone at the microseparator inlet with increasing flow rates.
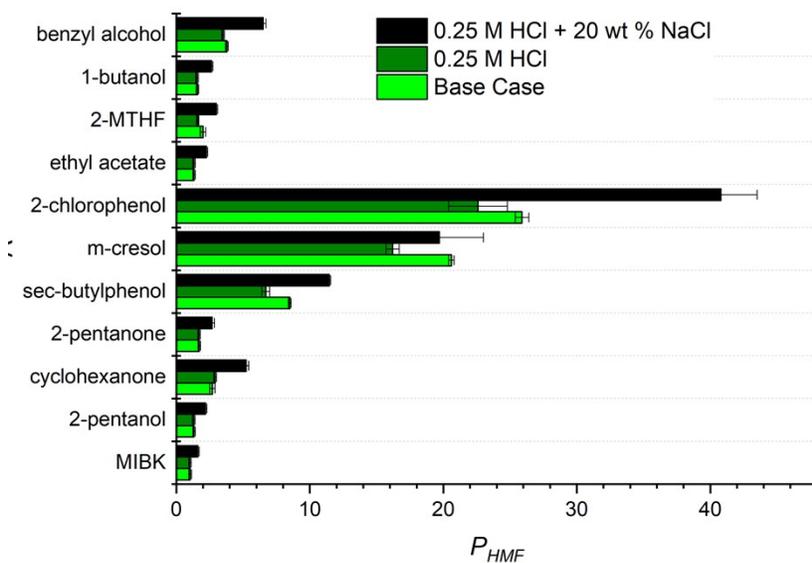
Figure S6. Effect of acid (0.25 M HCl) and salt (0.25 M HCl & 20 wt.% NaCl) addition on P_{HMF} in 11 solvent systems.

Figure S7. Effect of 0.25 M HCl addition on emulsion forming systems of m-cresol (left) and 2-chlorophenol (right).
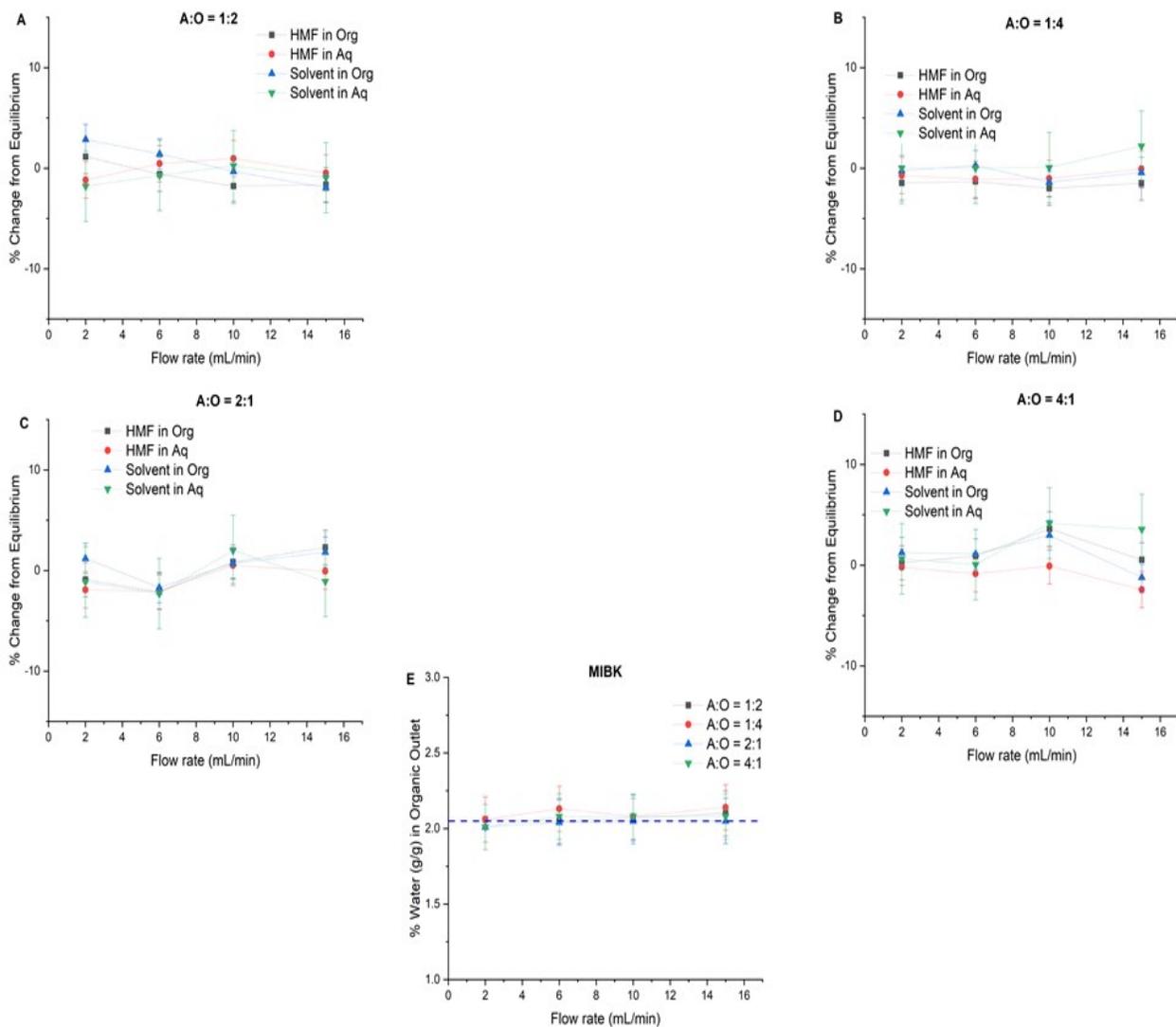
Figure S8. HPLC quantification of HMF and solvent concentration deviation at the microseparator outlets from the pre-equilibrated inlet phases for MIBK with **E)** the corresponding organic phase water content (KF) across a 1-15 mL/min flowrate range with aqueous to organic flow ratios of **A)** 1:2, **B)** 1:4, **C)** 2:1, and **D)** 4:1. The dotted blue line **(E)** indicates equilibrium water content in the organic phase. Error bars indicate total sampling and instrumental error.

9
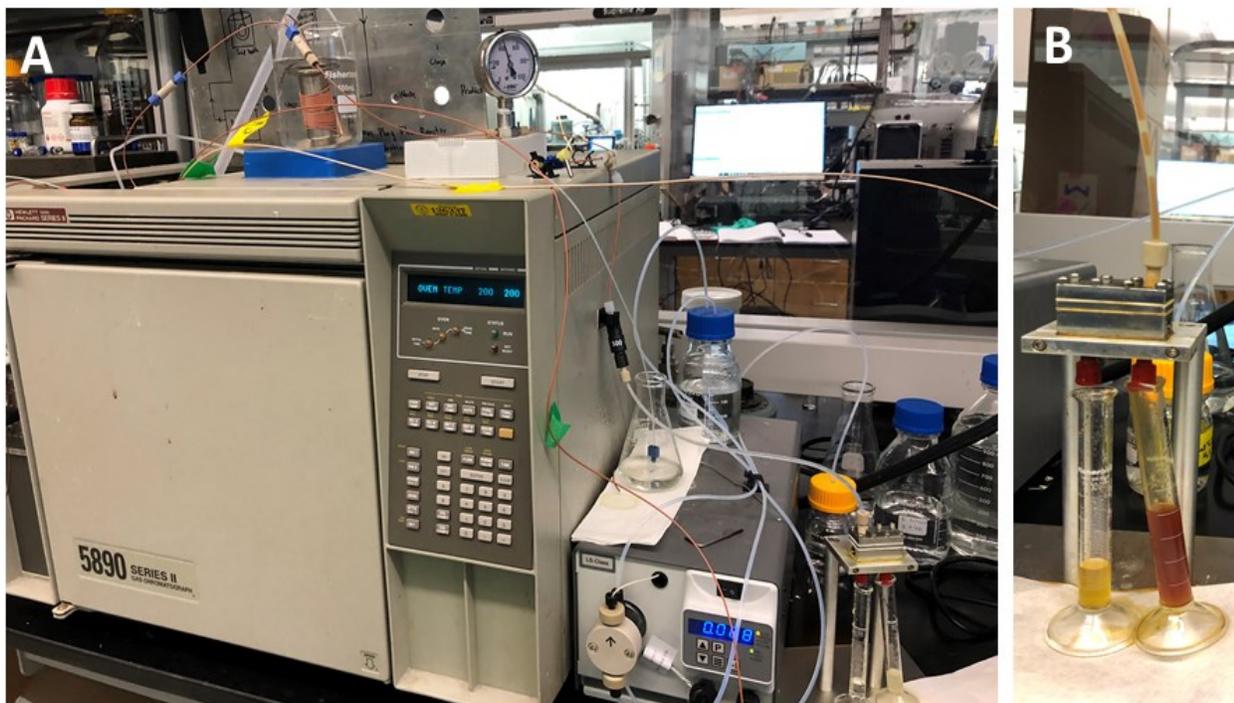
Figure S9. The integrated microreactor-microseparator setup (A) and a close up of the microseparator (B) showing perfect phase separation at 5 wt% fructose concentration and O:A=2. Segmented flow patterns in the inlet tubing to the microseparator are observed.
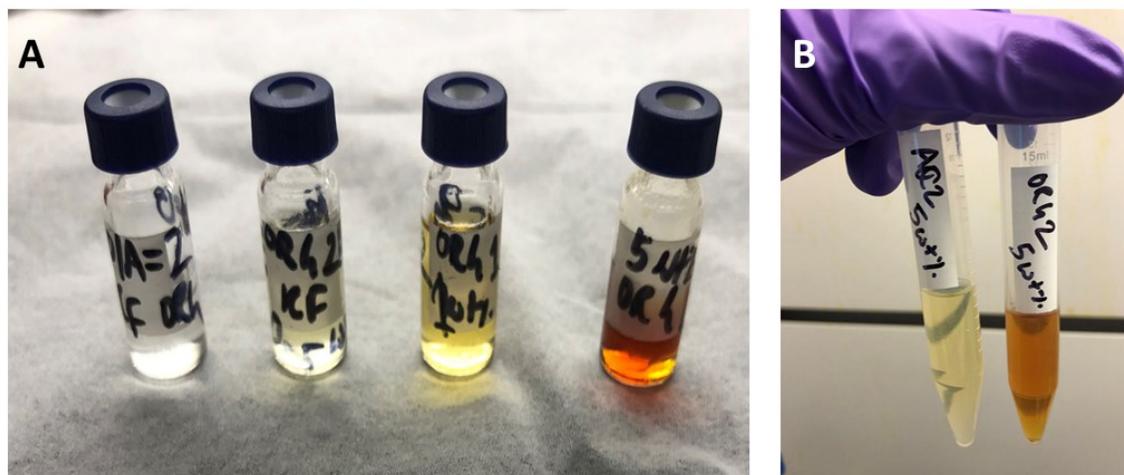
Figure S10. Organic phase collected at microseparator outlet showing color change (A) with increased initial fructose concentrations at 0.1 wt.%, 0.5 wt %, 1 wt.%, and 5 wt.% (left to right). Aqueous and organic outlet streams from the microseparator collected at 5 wt% fructose concentration (B).
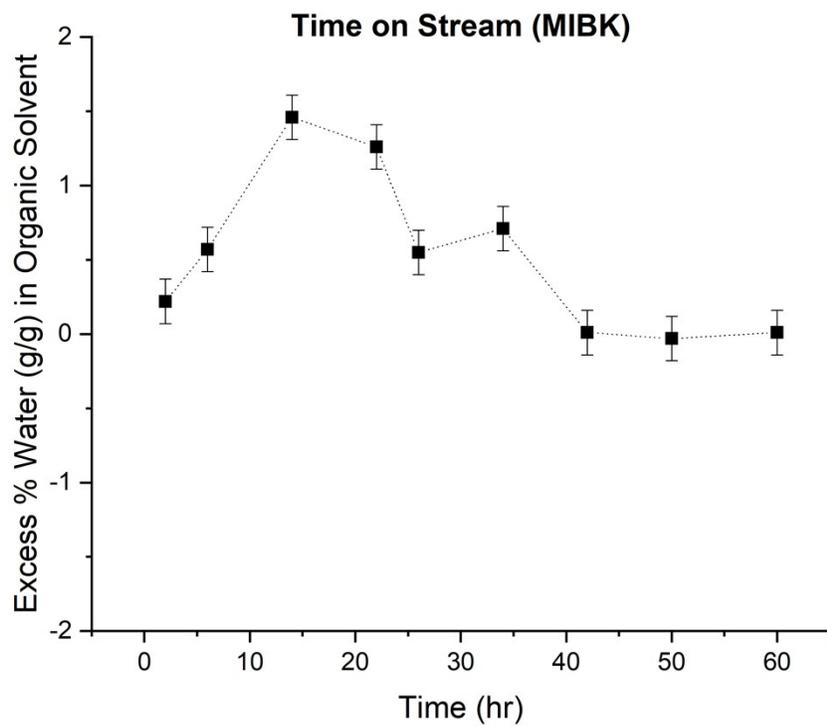
Figure S11. Time on stream experiments for the MIBK-water biphasic system at 1:1 flow ratio showing excess organic phase water content (KF) above equilibrium at the microseparator outlet for a continuous flow of 0.2 mL/min.
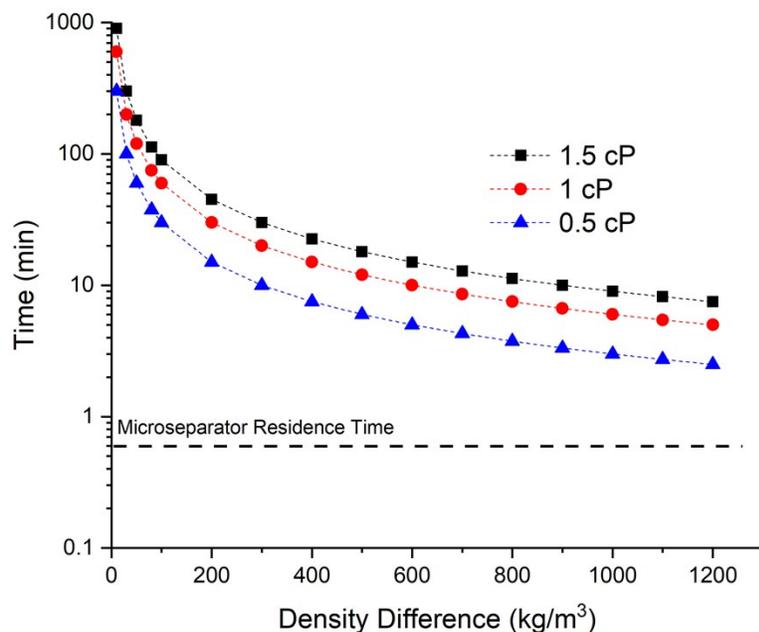
Figure S12. Estimated separation time for a gravity decanter with varying viscosity and phase density difference. The microseparator residence time here corresponds to a flow rate of 1 mL/min.

Supporting Tables

Table S1. List of Chemicals, Vendor, Product ID, and Purity.

Solvent Name	Vendor and Purity
1-butanol	Sigma-Aldrich, 99.5%
2-chlorophenol	Sigma-Aldrich, ≥99%
2-MTHF	Sigma-Aldrich, >99%
2-pentanol	Sigma-Aldrich, 98.0%
2-pentanone	Sigma-Aldrich, ≥99.5%
2-sec-butylphenol	Sigma-Aldrich, 98%
5-hydroxymethylfurfural	Sigma-Aldrich, 99%
acetonitrile	Fisher Chem. LC/MS Grade
cyclohexanone	Sigma-Aldrich, ≥99.0%
ethyl acetate	Sigma-Aldrich, 99.8%
m-cresol	Sigma-Aldrich, 99.0%

MIBK   Sigma-Aldrich, ≥98.5%

Table S2. Thermophysical Properties of 11 solvent systems investigated and heptane. Interfacial tension between the aqueous-rich and organic-rich phase of three systems (N/A) could not be measured.

Name	Viscosity (cP)	Interfacial Tension (mN/m)
Water	1.01	
MIBK	0.62	10.2
ethyl acetate	0.51	6.4
2-pentanol	3.6	3.5
heptane	0.387	50.71
benzyl alcohol	4.9	N/A
2-pentanone	0.56	5.55
2-MTHF	0.61	2.98
cyclohexanone	2.2	3.67
m-Cresol	6.8	N/A
2-secbutyl phenol	14.5	12.4
2-chlorophenol	5.5	N/A
1-butanol	3.1	1.9

Table S3. Effect of 20 % NaCl and 0.25 M HCl on P_{HMF} and phase miscibility.

	P_{HMF}	P_{HMF} (0.25 M HCl + 20 wt % NaCl)	% Water (organic phase)	% Water (organic phase) (0.25 M HCl + 20 wt % NaCl)
MIBK	1.04	1.61	2	1.72
2-pentanol	1.33	2.19	11.4	7.34
cyclohexanone	2.7	5.23	6.1	4.4
2-pentanone	1.72	2.67	4.13	2.49
2-secbutyl phenol	8.5	11.45	4.12	3.29
m-cresol	20.6	19.7	12.4	7.56
2-chlorophenol	25.9	40.8	11.4	5.9
ethyl acetate	1.33	2.25	3.35	N/A
2-MTHF	2	2.98	4.95	2.86
1-butanol	1.58	2.63	19.7	11.16
benzyl alcohol	3.78	6.5	10.33	5.78

Table S4. Experimental estimation of the microseparator dead volume.

Flowrate (mL/min)	Residence Time (sec)	Dead Volume (mL)
0.5	75	0.625
1	36	0.6