Model-based equipment design for the biphasic production of 5-hydroxymethylfurfural in a tubular reactor

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Abstract
Herein, a novel concept for the acid catalyzed dehydration of fructose (FRC) to 5-hydroxymethylfurfural (5-HMF) in a biphasic tubular reactor is presented. Reaction kinetic models were developed based on experiments performed in a newly developed lab-scale autoclave that enables a decoupled investigation of single-phase reaction and 5-HMF mass transfer. Our reaction kinetic models allow an accurate description of the biphasic reaction. Subsequently, we integrate the reaction kinetic models in the model-based design of a tailored reactor unit. This reactor unit employs the concept of in-situ extraction in a countercurrent flow of a monodisperse droplet swarm within a continuous aqueous phase. From reactor calculations, we obtain a maximum 5-HMF yield of 76% at full FRC conversion. Countercurrent in-situ extraction enables over 99% 5-HMF recovery in the organic phase.

1 | INTRODUCTION

The efficient production and purification of the important platform chemical 5-hydroxymethylfurfural (5-HMF) represents a challenging task. 5-HMF contains reactive alcohol and aldehyde functional groups leading to the formation of undesired byproducts, namely humins. Promising concepts envisage an integrated process of reaction and in situ extraction in order to increase the overall product yield. Torres et al. proposed a countercurrent Graesser extractor for the continuous production of 5-HMF from fructose (FRC). In their study, significant reduction of 5-HMF production costs can be achieved using the concept of countercurrent in-situ extraction. Recent experimental studies on the continuous production of 5-HMF in biphasic flow systems are conducted in microreactors. Shimanouchi et al. performed acid catalyzed FRC dehydration in a slug flow reactor with comparison to a conventional batch reactor. A similar approach was presented by Lieckgen et al. Both authors reported total 5-HMF yields in the range of 90%, however, a significant amount of 5-HMF remains in the aqueous phase at the end of reaction. Countercurrent in-situ extraction of 5-HMF enables to overcome this drawback by complete recovery of 5-HMF from the aqueous phase, thus facilitating downstream processing. In a recent review on continuous flow microreactors, Hommes et al. address remaining challenges regarding the capacity increase of microreactors towards the pilot or industrial scale. One challenge is to identify clogging of individual capillaries in a microreactor stack that requires selective solutions to counteract possible malfunctions. Larger reactor diameters that are typical for technical (0.05 m) and industrial scale extraction equipment (3–5 m) are an interesting alternative to provide robust operation.

Since solutions for technical and industrial scale intensified unit operations in the field of biomass conversion remain largely elusive, we propose an innovative concept for the continuous production of 5-HMF from FRC in a technical scale biphasic tubular reactor. We
perform a decoupled investigation of single-phase reaction and mass transfer to develop a model for this tubular reactor. Within this reactor model, we consider important technical aspects of biphasic fluid dynamics.

Several kinetic models for the acid catalyzed dehydration of FRC to 5-HMF and levulinic acid (LA) have been proposed. In our study, we use sulfuric acid (H₂SO₄), as this catalyst showed very good activity in previous investigations. The kinetic model for H₂SO₄ catalyzed FRC dehydration by Fachri et al covers a temperature range of T = (413 to 443) K while temperatures below 413 K were not investigated. Van Putten et al performed kinetic experiments for FRC dehydration catalyzed with H₂SO₄ at 410 K, yielding kinetic parameters for the formation of 5-HMF. However, side reactions to LA and humins were not modeled in their work.

To extend the data for the H₂SO₄ catalyzed FRC dehydration to even lower temperatures, we investigate the reaction in a temperature range of T = (378 to 408) K. We compare two different kinetic models differing in the description of the side reactions. Both models are extended by a detailed description of the extraction of 5-HMF from the aqueous phase into an organic solvent. In our study we use 2-methyltetrahydrofuran (2-MTHF) as solvent because it has advantageous attributes such as acidic stability, low boiling point and low ecotoxicity. Furthermore, the solvent system 2-MTHF/water features a stable miscibility gap in the temperature range of T = (293 to 423) K. The mass transfer model is developed by conducting extraction experiments at the relevant reaction temperatures.

Comprehensive models for biphasic tubular reactors for liquid-liquid reactions can be found in literature. These models have in common that the column is separated in several stages which are modeled as a cascade of ideally stirred tank reactors. It is typically assumed that the liquid phases are in equilibrium and hence mass transfer can be neglected. Moreover, fluid dynamics are not modeled in detail and the phase ratio in the reactor has to be estimated. Our herein presented model explicitly considers mass transfer as well as fluid dynamics in the biphasic countercurrent reactor.

2 EXPERIMENTAL

2.1 Chemicals

D-Fructose (FRC) (purity >99.5%) and 2-methyltetrahydrofuran (2-MTHF) (purity >99%) were purchased from Carl Roth GmbH (Karlsruhe, Germany). Sulfuric acid (H₂SO₄) (purity >96%) and formic acid (FA) (purity >98%) were purchased from Merck KGaA (Darmstadt, Germany). 5-hydroxymethylfurfural (5-HMF) (purity >99%) was purchased at AVA Biochemicals (Muttenz, Switzerland). Levulinic acid (LA) (purity >99%) was purchased from Sigma Aldrich (Steinheim, Germany). Water-free sodium sulfate (Na₂SO₄) (purity >99%) was purchased at VWR chemicals (Darmstadt, Germany). We used bidistilled water for all experimental solutions.

FIGURE 1 Hastelloy reactor for mass transfer and kinetic experiments: 1, 2: stirrer for organic and aqueous phase; 3: flow internals; 4: glass window; 5, 6: Raman and FT-IR probes; 7: sampling port; 8: inlet for HPLC pump [Color figure can be viewed at wileyonlinelibrary.com]

2.2 Experimental set up

All experiments are conducted in a custom made lab-scale reactor (premex GmbH, Lyss, Switzerland, see Figure 1). The design of the reactor is inspired by Nitsch et al. The nominal volume of the reactor is 0.5 × 10⁻³ m³. The reactor is equipped with two independent stirrers (1, 2) for the convection of the organic and aqueous phase. All biphasic experiments are conducted with a stable phase boundary, hence glass internals (3) are installed to provide stable flow conditions. Two glass windows allow visual control of the phase boundary (4). The vessel is manufactured from C-22 Hastelloy in order to withstand inorganic acids. The reactor has a maximum design temperature of 423 K and a maximum design pressure of 15 MPa. Temperature inside the reactor is measured with a type-K thermocouple. The reactor is equipped with a heating jacket that is controlled with a PID controller implemented in a custom made LabView program (ver. 2014 SP1, 32 bit). The PID controller allows temperature control with an accuracy of ±1.6 K. The thermocouple is calibrated in a range of T = (373 to 413) K against standard thermometers provided by Eichamt Wertheim (Wertheim, Germany). A pressure transducer (model A-20-S, WIKA, Klingenberg, Germany) is used to measure the system pressure. The pressure transducer is calibrated in a range of P = (0.1 to 1) MPa using a dead weight tester RKII (Debro Messtechnik GmbH, Meerbusch, Germany). An HPLC pump (Azura P4.5, Knauer Wissenschaftliche Geräte GmbH, Berlin, Germany) is used to inject the substrate solution (8). To provide stable flow conditions for the pump, a back-pressure regulating valve (JR-BPR2, Knauer Wissenschaftliche Geräte GmbH, Berlin, Germany) is installed. A detailed flow sheet of the entire experimental set-up can be found in section 1 of the Supporting Information.
2.3 | Experimental procedure

Investigations on the reaction kinetics of FRC dehydration are performed in aqueous solutions with H$_2$SO$_4$ as catalyst. In addition to experiments starting from FRC as substrate, we also perform experiments with a mixture of FRC and 5-HMF. The following protocol is applied for a typical experiment: The aqueous solution with a defined amount of catalyst is weighed into the autoclave. The velocity of the lower stirrer is set to 200 rpm and the aqueous solution is heated to a desired temperature. After the temperature is reached and stable for 1 hr, the substrate solution is injected with the HPLC pump system at a constant flow of 3 x 10$^{-7}$ m$^3$/s. Based on the desired initial substrate concentration, the time for injection is adjusted. Immediately after the injection, samples are taken for HPLC analysis. Details on HPLC analysis can be found in section 2 of the Supporting Information.

In our investigations, concentrations of reactants and products are small on a molar basis. Therefore, we neglect changes in total liquid volume due to water formation of the dehydration reaction. We give attention to the volume of each sample being always in the range of 0.1% of the total liquid volume in the autoclave. In order to minimize the sampling error caused by residual liquid in the tubing of the sampling port, air from the sampling syringe is used to flush the sampling port.

To determine the influence of temperature and the presence of SO$_4$$^{2-}$-anions on the partition coefficient of 5-HMF in the biphasic system 2-MTHF/water, we perform equilibrium measurements in our experimental set-up (see Figure 1) applying the following protocol: A defined amount of water, 5-HMF, 2-MTHF and optionally Na$_2$SO$_4$ is weighed into the autoclave. The velocity of the lower and upper stirrer is set to 200 rpm to facilitate fast equilibration and the autoclave is heated to a desired temperature. Once the desired temperature is reached, the organic phase is analyzed with Raman spectroscopy. Spectra acquisition is performed every 5 min for a total period of 1 hr or until no further change in the Raman signal is detected. Once this state is reached, samples of the aqueous phase are taken for HPLC analysis.

Mass transfer experiments follow the same protocol with some additional features: The solvent 2-MTHF is used in biphasic experiments. The lower and upper stirrer are set to stirrer velocities that meet the constraint of equal Reynolds (Re) numbers in both liquid phases. Every mass transfer experiment is performed at a stable phase boundary between both liquids which can be calculated from the diameter of the autoclave. An aqueous solution containing water and a defined amount of 5-HMF is injected into the aqueous phase. After injection, the organic phase is analyzed inline with Raman spectroscopy. The aqueous phase is analyzed inline with FT-IR spectroscopy. Details on FT-IR and Raman analytics can be found in section 2 of the Supporting Information. Biphasic reaction experiments are performed similar to mass transfer experiments, with H$_2$SO$_4$ added to the aqueous phase. The substrate in these experiments is FRC and the aqueous phase is sampled according to single-phase experiments.

3 | MODELING

3.1 | Single-phase reaction kinetics

Experimental and modeled concentration data is used to calculate the conversion of FRC ($X_{FRC}$), and selectivity ($S_i$) and yield ($Y_i$) of the detectable products in the HPLC analysis according to the following equations:

$$X_{FRC} = \frac{(n_{FRC,0} - n_{FRC,i})}{n_{FRC,0}}$$

$$S_i = \frac{(n_i - n_{i,0})}{(n_{FRC,0} - n_{FRC,i})}$$

$$Y_i = X_{FRC} \cdot S_i$$

with $n_i$ being the molar quantity of detectable species $i$, in our case FRC, 5-HMF, LA, and FA. Our experimental procedure does not allow for quantification of soluble and insoluble byproducts from FRC dehydration (humins) by spectroscopy or HPLC analysis. Therefore, we calculate the volume specific mass of carbon $m_{carbon,humins}$ based on humins’ production during FRC dehydration based on a carbon balance similar to $^{20}$:

$$m_{carbon,humins} = C_{feed} \cdot M_{carbon,feed} - \sum_i C_i \cdot M_{carbon,i}$$

Values for $C_{feed}$ and $C_i$ are obtained from experimentally determined and modeled concentrations. $M_{carbon,feed}$ and $M_{carbon,i}$ are the specific molar mass for carbon in the feed and each detectable species $i$. To evaluate the performance of the biphasic tubular reactor, we calculate the absolute mass of carbon assigned to humins $m_{carbon,humins}$ for both liquid phases $k$ (index $aq$ denotes the aqueous phase, index $org$ denotes the organic phase)

$$m_{carbon,humins} = C_{feed} \cdot M_{carbon,feed} \cdot V_{aq} - \sum_i \sum_k C_i \cdot M_{carbon,i} \cdot V_k$$

The respective total carbon yield is calculated with

$$Y_{carbon} = \left(1 - \frac{m_{carbon,humins}}{C_{feed} \cdot M_{carbon,feed} \cdot V_{aq}}\right) \times 100\%.$$

We compare two different reaction pathways in this work to describe the time-dependent concentration profiles of the single-phase reaction (see Figure 2). Details on the system of rate equations for both models and the formulation of the system of ordinary differential equations (ODE) can be found in section 3 of the Supporting Information. Parameter values for pre-exponential factors and activation energies are determined using the MATLAB software package (build 2018Ra). We perform a least squares minimization between experimental and modeling data using the lsqnonlin function. Following the approach proposed by Fachri et al $^{10}$ concentrations of FRC,
5-HMF, and LA are used for parameter regression. Regression is done simultaneously for all conducted experiments. Confidence intervals (95%) are calculated based on the nonlinear parameter estimates using the \( \text{nlparci} \) function implemented in the MATLAB Statistics Toolbox.\(^{21}\)

The structure of Model 2 is adopted from a previously proposed kinetic model by Fachri et al.\(^{10}\) Humins formation is modeled with two independent side reactions starting from FRC and 5-HMF as substrates. In contrast to Fachri et al, we use orders of 1 for the concentrations of FRC, 5-HMF, and \( \text{H}_2\text{SO}_4 \). Previous work by van Zandvoort et al\(^{22}\) confirms that byproduct formation during the acid catalyzed dehydration of sugar to 5-HMF is mostly influenced by temperature and to a lower extend by acid and substrate concentration. Körner et al\(^{23}\) investigated the effect of different Brønsted acids on the selectivity of 5-HMF during hydrothermal conversion of FRC at 413 K. They conclude that 5-HMF yield is unaffected by the pH value.

The structure of Model 1 is based on the description of the formation of humins via a coupled side reaction between FRC and 5-HMF. Patil et al\(^{24}\) performed a comparison of humins formed from glucose, FRC and 5-HMF and found that each of these reactants must be converted to an intermediate (2,5-dioxo-6-hydroxyhexanal) to enable humins formation via aldol addition. Based on these findings, they state that direct formation of humins from FRC is insignificant.\(^{24}\)

Investigations on 5-HMF formation in absence of water where 5-HMF is assumed to be stable also show that humins production is suppressed.\(^{25-27}\)

3.2 | Calculation of partition coefficients and modeling of mass transfer

The calculation of the mass transfer rate requires knowledge of the equilibrium state which can be represented by the partition coefficient \( K \). We calculate \( K \) based on data obtained in the equilibrium measurements described in Section 2.3 with

\[
K = \frac{C_{\text{HMF,org}}^{\text{eq}}}{C_{\text{HMF,aq}}^{\text{eq}}}.
\]

The concentration of 5-HMF in the aqueous phase \( C_{\text{HMF,aq}}^{\text{eq}} \) is directly obtained from HPLC measurements. Raman spectroscopy is calibrated in mole fractions, hence the measured data has to be multiplied with the respective molar density of the organic phase at the respective temperature. To account for the temperature sensitivity of the molar density in the binary system 2-MTHF/water, we use the PC-SAFT 6P model from\(^{28}\) in Aspen Plus ver. 8.8.\(^{29}\) 5-HMF mole fractions in the organic phase are in the range of 1 mol%. Assuming an

![FIGURE 2](image-url) Kinetic models used in this work to describe the single- and biphasic reaction. Model 1 with second order side reaction (this work) and Model 2 with two independent first order side reactions (according to Reference 10)
ideal mixture we estimated the influence of 5-HMF on molar density of the organic phase to be less than 0.5%.

The change in 5-HMF concentration due to mass transfer in both the aqueous and organic phase can be calculated with

\[
\frac{\partial C_{\text{HMF,aq}}}{\partial t} = -R_{5\text{-HMF}} = k_{\text{od}} \cdot a \cdot (K \cdot C_{\text{HMF,aq}}(t) - C_{\text{HMF,org}}(t)) \quad (8)
\]

\[
\frac{\partial C_{\text{HMF,org}}}{\partial t} = -R_{5\text{-HMF}} = k_{\text{od}} \cdot a \cdot (K \cdot C_{\text{HMF,aq}}(t) - C_{\text{HMF,org}}(t)) \quad (9)
\]

Similar to Raman spectroscopy, FT-IR spectroscopy is calibrated in mole fractions. To obtain values for \(C_{\text{HMF,aq}}\) we multiply the measured mole fractions with the molar density of the aqueous phase at the respective temperature using the PC-SAFT 6P model in Aspen Plus ver. 8.8.28 We use values for the partition coefficient \(K\) at 383 and 393 K from equilibrium measurements. The mass transfer rate \(R_{5\text{-HMF}}\) is calculated from the interfacial area for mass transfer per unit volume \(a\) and the overall mass transfer coefficient \(k_{\text{od}}\). All mass transfer experiments are performed at a stable phase boundary, hence the interfacial area for mass transfer per unit volume can be calculated from the autoclave’s diameter \(D_a\) and the liquid volume \(V_{\text{org}}\) of the organic phase.

\[
a = \frac{D_a^2 \cdot \pi}{4 \cdot V_{\text{org}}(T)} \quad (10)
\]

To account for the change in \(V_{\text{org}}\) with increasing temperature, we use the PC-SAFT 6P model from 28 to calculate \(V_{\text{org}}\) at 383 and 393 K.

Values for \(k_{\text{od}}\) are determined via least squares minimization in MATLAB.21 Both differential Equations (8) and (9) are solved using the ode45 solver.21 Initial concentrations for \(C_{\text{HMF,aq}}(t = 0)\) and \(C_{\text{HMF,org}}(t = 0)\) are obtained from measured data in the aqueous and organic phase. We solve the following optimization problem using the fminsearch function in MATLAB.

\[
\min_{k_{\text{od}} \in \text{parameters}} \sum_{n=1}^{n_{\text{total}} \times 2} \left[ (C_{\text{HMF,aq,calc}} - C_{\text{HMF,aq,meas}})^2 + (C_{\text{HMF,org,calc}} - C_{\text{HMF,org,meas}})^2 \right].
\]

(11)

with \(n_{\text{total}}\) being the total number of experimental data points for each individual experiment.

Mass transfer experiments are performed at equal Reynolds numbers in both the aqueous and the organic phase. The Reynolds number is calculated from

\[
Re = \frac{d_s^2 \cdot N}{\nu}.
\]

The diameter \(d_s\) of the stirrer is 0.04 m. The rotational speed \(N\) of the stirrer is varied for different experiments. Details on the calculation of the kinematic viscosity \(\nu\) for the organic and aqueous phase as a function of temperature are given in section 4 of the Supporting Information.

### 3.3 Reactor model development

We present a model for a biphasic tubular reactor, in which the dehydration reaction of FRC to 5-HMF (see Section 3.1) and the product extraction (see Section 3.2) are simultaneously conducted. At the top of the tubular reactor, the aqueous phase (index c) enters the reactor (see Figure 3) and the organic phase (index d) is inserted as droplets at the bottom of the tubular reactor. The droplets then rise inside the continuous aqueous phase to the top. The continuous phase is flowing to the bottom, thus resulting in a countercurrent mode of operation. Calculation of the spatial concentration profiles in both liquid phases is done by solving a set of one-dimensional rate equations.

To account for a fast calculation of the rate model, we developed a two step simulation approach. In the first step, the stationary and fully developed fluid profile is calculated (see Section 3.3.1). In the second step, the dynamic concentration profile in the extraction column is simulated (see Section 3.3.2). The pipe cross-section area \(A_R\) of the simulated reactor can be calculated from its diameter \(D = 0.05\) m. Reactor height is set to provide the necessary residence time to obtain at least 97% conversion of the substrate. The ratio of the

![FIGURE 3 Schematic of the counter-current tubular reactor](Color figure can be viewed at wileyonlinelibrary.com)
volume flows of disperse $\dot{V}_d$ and continuous phase $\dot{V}_c$ is set to 3.2 according to.\textsuperscript{20}

### 3.3.1 | Fluid dynamics

We consider monodisperse droplets with a diameter of $d_0 = 2.8$ mm for our calculations. The droplet diameter is determined in experiments conducted in a technical scale tubular reactor. According to Goedecke, this droplet diameter is in the range of droplet diameters in technical extraction equipment.\textsuperscript{9} For details on the experimental setup and the procedure applied to determine the droplet diameter refer to section 5 of the Supporting Information. The droplet diameter is determined at three different heights of the reactor to account for a possible droplet-droplet coalescence behavior of the biphasic system 2-MTHF/water. In our experiments no significant increase in droplet diameter caused by high coalescence rates is observed. In case of high coalescence rates or a higher reactor length, internals like stirred compartments\textsuperscript{31} or pulsed sieve trays\textsuperscript{32} allow stabilization of the droplet diameter.

To reduce the complexity of the system, we assume no internal circulation inside the droplets occurs and the droplets do not deform.\textsuperscript{32} For this case, the free sedimentation velocity $V_0$ of a single droplet is only dependent on the two liquid phase's densities $\rho_c$ and $\rho_d$, the droplet diameter $d_0$, and the drag coefficient $c_D$. The velocity is then calculated from\textsuperscript{32}:

$$V_0 = \sqrt{\frac{4}{3} \frac{\rho_c - \rho_d}{\rho_c} \frac{g d_0^3}{c_D}}.$$  \hspace{1cm} (13)

where the drag coefficient $c_D$ is given by

$$c_D = \frac{432}{Ar} + \frac{20}{Ar^2} + \frac{0.51}{140 + Ar^2}.$$  \hspace{1cm} (14)

and the Archimedes number $Ar$ reads

$$Ar = \frac{\rho_c - \rho_d}{\rho_c} \frac{g d_0^3}{\eta_c^2}.$$  \hspace{1cm} (15)

with $\eta_c = 2.44 \times 10^{-4}$ Pa s being the continuous phase's dynamic viscosity. Values for $\rho_c = 968.98$ kg/m$^3$ and $\rho_d = 764.10$ kg/m$^3$ were determined in Aspen Plus ver. 8.8.\textsuperscript{24} In a counter-current tubular reactor, droplets are rising as a droplet swarm. Due to interactions between droplets, the velocity of droplets in a swarm is usually lower than the velocity of a single droplet. Richardson and Zaki\textsuperscript{33} propose a model to describe the relative swarm velocity $v_{rs}$ as a function of the free sedimentation velocity $V_0$ and the dispersed-phase hold-up $\epsilon = 0.03$ modified by the swarm exponent $n = 4.65$:

$$v_{rs} = V_0 (1 - \epsilon)^{n-1}.$$  \hspace{1cm} (16)

The kinematic relationship of a droplet swarm and the absolute velocities of the continuous $v_{abs,c} = v_c (1 - \epsilon)^{-1}$ and disperse phase $v_{abs,d} = v_d \cdot \epsilon^{-1}$ is given by the difference of the relative swarm velocity and the absolute velocity in the continuous phase. Assuming a monodisperse and homogeneous droplet distribution in the reactor, we are able to describe the absolute phase velocities as a function of the superficial velocities $v_c = V_c / A_R$ and $v_d = V_d / A_R$ and the dispersed-phase hold-up:

$$v_0 \cdot (1 - \epsilon)^{2.65} = \frac{V_d}{\epsilon} \cdot \frac{v_c}{1 - \epsilon} = \frac{4}{\pi D^2} \left( \frac{V_d V_c^{-1} - \frac{1}{1 - \epsilon}}{\epsilon} \right).$$  \hspace{1cm} (17)

Consequently, the fluid dynamics are specified by Equations (13)-(15) and (17), correlating the fluid dynamic and process parameters.

### 3.3.2 | Concentration profile

The temporal behavior of the spatial concentration profile is modeled by the partial differential equation system

$$\frac{\partial c_{HMF}}{\partial t} = \frac{\partial}{\partial z} \left( D_{axc} \frac{\partial c_{HMF}}{\partial z} \right) + \frac{\partial}{\partial z} \left( -v_{rs} \frac{\partial c_{HMF}}{\partial z} + \frac{n_{HMF}}{V_c} \right)$$  \hspace{1cm} (18)

$$\frac{\partial c_{HMF}}{\partial t} = \frac{\partial}{\partial t} \frac{\partial}{\partial z} \left( -v_{rs} \frac{\partial c_{HMF}}{\partial z} + \frac{n_{HMF}}{V_c} \right)$$  \hspace{1cm} (19)

On the left hand side of the equation, the change of concentration per time is given. The first term on the right hand side describes the mass transport due to convection in axial direction of the column. The corresponding velocities of the continuous and disperse phase result from the calculation of the fluid dynamics. The second term on the right hand side of Equations (18) and (19) describes the mass transport due to axial back mixing or dispersion, which is physically generated by the flow of the droplets within the continuous phase. The axial dispersion coefficient $D_{axc}$ is usually obtained from experiments in a technical scale set-up.\textsuperscript{5} Correlations for the axial dispersion coefficient are often erroneous,\textsuperscript{32} therefore we set $D_{axc} = 0$ m$^2$/s. This value for $D_{axc}$ represents an idealized condition for the flow in the continuous phase. Based on a sensitivity study varying $D_{axc}$ in a technical relevant range for stirred and sieve tray columns, we hold this assumption valid. A calculation using a maximum value of $D_{axc} = 3.5 \times 10^{-4}$ m$^2$/s proposed by Henschke\textsuperscript{32} for pulsed sieve tray columns shows a variation in 5-HMF yield of less than 1%.

The third terms on the right hand side of Equations (18) and (19) are source terms as $r_d$ designates the reaction rate of the particular component. Depending on the reaction kinetic mechanism of the dehydration reaction and the mass transfer rate $n_{HMF}$ (see Equation (21)), the amount of 5-HMF transferred between the two phases can be calculated. The definition of the mass transfer rate
\[
\dot{n}_{\text{HMF}}(z,t) = A_{\text{mt}} k_{\text{od}} [K C_{\text{HMF}},(z,t) - C_{\text{HMF}},(z,t)]
\]  

(21)

requires the mass transfer coefficient \( k_{\text{od}} \) obtained from mass transfer experiments and the available surface of the dispersed phase \( A_{\text{mt}} \), which is determined by the drop size and the dispersed phase holdup.

Due to the nonlinear source terms occurring in the first reaction kinetic model, deriving an analytical solution of the coupled PDE system is impossible. Therefore, we semi-discretize the PDE system in space to obtain an ordinary differential equation (ODE) system in time.\(^{34}\) As the space-discretization leads to an ill-conditioned block triagonal matrix depending on the mesh size of the discretization, the resulting ODE system is stiff.\(^{34}\) We use the MATLAB solver \texttt{ode15s},\(^{21}\) which is based on an implicit Runge-Kutta method, to solve these ODEs.

4 | RESULTS AND DISCUSSION

4.1 | Single-phase reaction

We performed a total of nine experiments in order to obtain kinetic parameters for Model 1 and Model 2. Details on the conditions for all conducted experiments can be found in section 6 of the Supporting Information. The maximum 5-HMF yield obtained from single-phase experiments in this work is 39% at 398 K and \( C_{\text{H2SO4}} = 0.18 \text{ kmol/m}^3 \) at 70% conversion. Figure 4 depicts all experimental yields from this work as a function of FRC conversion. Results were obtained from all experiments starting from FRC as substrate. Van Putten et al\(^{1}\) investigated FRC dehydration at 410 K and comparable concentrations of \( \text{H}_2\text{SO}_4 \) and report a yield around 40% at 80% conversion. Based on kinetic parameters by Körner et al\(^{23}\), a maximum 5-HMF yield of 40% at 83% conversion can be obtained. Fachri et al\(^{10}\) report slightly higher yields of 45% at 413 K and \( C_{\text{H2SO4}} = 0.1 \text{ kmol/m}^3 \).

Results for an exemplary single-phase experiment together with model predictions are shown in Figure 5. The concentration profiles show the characteristic trend of a sequential reaction according to Reference 35. Both Model 1 and Model 2 are able to describe these trends with comparable accuracy. The calculated volume specific mass of carbon assigned to humins formation (see Equation (4)) is also captured well by both models.

In addition to experiments starting from FRC as substrate, we also performed experiments starting from a mixture of FRC and 5-HMF. The rational behind these experiments is to provide high initial concentrations of FRC and 5-HMF in order to trigger a possible coupled side reaction (see Model 1). In Figure 6, FRC concentration decreases in time while 5-HMF remains at a nearly constant level in the first 20–30 min. Apparently, the rate of 5-HMF formation and its transformation to LA and humins are equal in this phase of the reaction. After 30 min, 5-HMF concentration starts decreasing. The concentration of LA increases by a nearly linear trend. Similar to the experiment starting from FRC, both kinetic models allow an accurate description.
of the detectable species as well as the calculated volume specific mass of carbon assigned to humins formation. Parity plots for all experimental and modeled data obtained in this work is shown in section 7 of the Supporting Information.

A comparison of the obtained kinetic parameters for both kinetic models along with parameters reported in literature is done in the following. Table 1 lists the parameters for both kinetic models developed in this work compared with parameters from Fachiri et al.\textsuperscript{10} Girisuta et al.\textsuperscript{36} and van Putten et al.\textsuperscript{1} The values for the activation energy \(E_F\) for both kinetic models developed in this work are in good agreement to parameter values found for the reaction catalyzed by \(\text{H}_2\text{SO}_4\). The activation energy \(E_{2FH}\) for the humins formation of Model 1 is significantly higher compared to Model 2 and literature values from.\textsuperscript{10} This is probably due to the coupling of both FRC and 5-HMF concentration to describe the side reaction.

The activation energy \(E_{2FH}\) for the side reaction of Model 2 is in better agreement to the parameter by Fachiri et al.\textsuperscript{10} Activation energies \(E_{1H}\) for the reaction of 5-HMF to LA are also in good agreement to values reported by.\textsuperscript{10,36} Both our values for \(E_{1H}\) (Model 1 and Model 2) are close to the parameter by Girisuta et al.\textsuperscript{36} where only rehydration of 5-HMF in absence of FRC was investigated. A comparison of the pre-exponential factors leads to a similar conclusion. Values for the main reactions are all in good agreement, while values for the side reactions diverge and usually have the highest uncertainties.

We assume that a possible reason for the insufficient modeling of the side reactions is missing data for concentration of different byproduct species that cannot be taken into account for the parameter regression. During HPLC analysis we observed additional peaks that could be attributed to several side products. However, fractionation and calibration of these components was not possible. Moreover, also solid products form during the reaction that precipitate and hence are hard to quantify during reaction. Fachiri et al.\textsuperscript{10} reported similar issues with quantification of soluble and insoluble humins in their studies.

### 4.2 Partition coefficients and mass transfer

Experimental results of partition coefficients determined in this work are depicted in Figure 7. The corresponding tabulated data can be found in section 8 of the Supporting Information. The experimental value for the partition coefficient determined in this work at 293 K is \(K = 2.2\), and comparable to a recently reported value \((K = 1.9)\) for the solvent system 2-MTHF/water by.\textsuperscript{20} To account for the salting-out effect of \(\text{SO}_4^{2–}\) anions introduced by the presence of \(\text{H}_2\text{SO}_4\) in the reactive system, we add \(\text{Na}_2\text{SO}_4\) to the ternary system 2-MTHF/water/5-HMF. In a detailed study on anion and cation effects on 5-HMF partitioning in the solvent system methyl isobutyl ketone (MIBK)/water, Mohammad et al.\textsuperscript{37} find that the salting-out effect on partitioning of 5-HMF mainly depends on the anion species and only marginally on the type of cation.

Addition of \(\text{Na}_2\text{SO}_4\) at 293 K leads to an increase in the partition coefficient. A similar effect on partitioning of 5-HMF caused by the addition of \(\text{Na}_2\text{SO}_4\) has been reported by Mohammad et al.\textsuperscript{37} for the solvent system MIBK/water at 298 K. Increasing temperature leads to decreasing partition coefficients for all investigated concentrations of \(C_{\text{SO}_4^{2–}}\) (Figure 7). A possible explanation for this behavior is the increase in mutual solubility with increasing temperature in the solvent system 2-MTHF/water. Roman-Leshkov et al.\textsuperscript{30} conducted an extensive study on the effect of partition coefficients on 5-HMF selectivity in biphasic systems. They find that some solvent systems with high partition coefficients at room temperature yield lower 5-HMF selectivities at elevated temperatures. They explain this effect with an increase in mutual solubility of the respective biphasic solvent systems, resulting in a decrease of the partition coefficient of 5-HMF. Weingart et al.\textsuperscript{38} report a similar effect for the solvent system hexafluorisopropanol/water. For the solvent system 2-MTHF/water, Glass et al.\textsuperscript{13} find that mutual solubility also increases with temperature. We therefore assume this behavior of the solvent system 2-MTHF/water to be the reason for the temperature sensitivity of the 5-HMF partition coefficient. In the following, the obtained partition

| Parameter | Model 1 (this work) | Model 2 (this work) | Reference 10 | Reference 36 | Reference 1 |
|-----------|---------------------|---------------------|--------------|--------------|-------------|
| \(E_F\)   | 127 ± 5             | 126 ± 9             | 123 ± 5      | –            | 124 ± 22    |
| \(E_{2FH}\)| 200 ± 20            | 131 ± 12            | 148 ± 12     | –            | –           |
| \(E_{1H}\) | 101 ± 1             | 106 ± 12            | 92 ± 5       | 110 ± 0.7    | –           |
| \(E_{2H}\) | –                   | 111 ± 7             | 119 ± 10     | 111 ± 2      | –           |
| \(kR_{1F}\) | 1.01 ± 0.1          | 0.9 ± 0.16          | 1.1 ± 0.1    | –            | 0.9 ± 0.1   |
| \(kR_{2FH}\)| 5.45 ± 1.8         | 0.37 ± 0.17         | 0.55 ± 0.1   | –            | –          |
| \(kR_{1H}\) | 0.35 ± 0.06         | 0.34 ± 0.1          | 0.38 ± 0.04  | 0.34 ± 0.01  | –          |
| \(kR_{2H}\) | –                   | 0.14 ± 0.18         | 0.142 ± 0.04 | 0.117 ± 0.008| –          |

**TABLE 1** Kinetic model parameters for the \(\text{H}_2\text{SO}_4\) catalyzed dehydration of FRC to 5-HMF. Parameters for Model 1 and Model 2 are obtained in this work. Note that only absolute values of activation energies and pre-exponential factors are compared since reaction orders in this work are set to 1. According to the selected references, the unit of the equivalent reaction rate is \([\text{mol}/\text{L}.\text{min}]\) and the unit of the activation energy is \([\text{kJ/mol}]\).
coefficients are used as parameters in modeling of mass transfer and biphasic reaction.

Mass transfer of 5-HMF from the aqueous into the organic phase is investigated decoupled from reaction. We performed mass transfer experiments in the temperature range relevant for reaction. Figure 8 depicts an experiment performed at 393 K. The obtained values for $k_{od}$ are listed in Table 2. For each experiment we calculated the molar balance in 5-HMF based on the molar amount of 5-HMF in both liquid phases compared to the initial amount injected into the system. Our mean error in the component balance for all conducted experiments is below 5%.

With increasing Reynolds numbers, $k_{od}$ increases with an exception at $Re = 6,399$ at 393 K. Kalem determined mass transfer coefficients in the ternary system toluene/water/acetone at 298 K in an apparatus with the same geometry as the autoclave used in this work. These mass transfer coefficients are in a range of $2.3 \times 10^{-5}$ to $4.7 \times 10^{-5}$ m/s and thus comparable to our derived values. For further application at 388 K we use a value for $k_{od}$ derived from linear interpolation between 393 and 383 K at $Re = 8,532$.

4.3 | Biphasic reaction

In order to validate both models with respect to their performance in the biphasic reaction, a biphasic experiment is conducted according to Section 2.3. Prediction of the experimental results is performed with a combination of the reaction kinetic and mass transfer model developed in Section 4.1 and Section 4.2. The experiment is performed at $Re = 8,532$ and 388 K which yields a value for $k_{od,Re = 8,532} = 7.68 \times 10^{-5}$ m/s. The partition coefficient at 388 K and $C_{SO_2^=} = 0.16\text{kmol/m}^3$ obtained from linear interpolation of experimental data is set to $K = 1.35$. We do not adjust any further parameters to describe the biphasic reaction. The experimental and modeling data for the time-dependent concentration profiles in the biphasic reaction are depicted in Figures 9 and 10. The FRC conversion reaches approximately 50% after 60 min which is described well by Model 1. The formation of 5-HMF in the aqueous phase is suppressed.

### Table 2: Mass transfer coefficients $k_{od}$ for different Re-numbers

| $T$/K | Re | $k_{od}$/m/s |
|-------|----|--------------|
| 383   | 4,266 | $3.30 \times 10^{-5}$ |
|       | 6,399 | $5.40 \times 10^{-5}$ |
|       | 8,532 | $6.44 \times 10^{-5}$ |
| 393   | 4,266 | $6.36 \times 10^{-5}$ |
|       | 6,399 | $5.51 \times 10^{-5}$ |
|       | 8,532 | $6.93 \times 10^{-5}$ |
by the simultaneous extraction into the organic phase. This effect is captured accurately by both models, as well as the formation of LA and FA. The calculated mass concentration of carbon assigned to humins formation is described well by Model 1. Model 2 overpredicts humins formation which can be explained with the parallel side reaction from FRC. This side reaction is also the reason for the faster decrease in FRC concentration compared to the experimental data.

The experimental data in the organic phase (Figure 10), show a steady increase in 5-HMF concentration. At the beginning of the extraction into the organic phase (0–10 min), we observe a sigmoidal trend of the concentration data. Both kinetic models capture this trend accurately. The sigmoidal trend can be explained by mass transfer limitation for the extraction of 5-HMF from the aqueous into the organic phase in this conducted experiment. In accordance to the mass transfer experiments, the biphasic reaction is also performed in a flow regime with a defined phase boundary. Due to the small specific area for mass transfer, the resulting mass transfer rate is consequently small compared to the rate of 5-HMF formation. To support this assumption we compared the calculated rate of 5-HMF formation and the calculated rate of 5-HMF mass transfer for the biphasic experiment (see section 9 of the Supporting Information). Over the entire course of the experiment, the 5-HMF formation rate significantly exceeds the rate of mass transfer.

At long reaction times both models overpredict the 5-HMF concentration in the organic phase. The concentration in the organic phase is measured with inline Raman spectroscopy. At reaction times longer than 20 min, we find an increase in scattering of the data compared to the data in the range of 0–20 min. We assume this is due to a fluorescence effect caused by soluble humins species. This fluorescence effect corrupts the signal and can lead to an erroneous quantification of 5-HMF. Considering that our kinetic models were not adjusted to the experimental data of the biphasic reaction, the quality of the model prediction is acceptable. In the following, we will use both reaction kinetic models developed in this work to describe the reaction in a single and biphasic tubular reactor.

The results from the modeled selectivity of the single-phase reaction are depicted in Figure 11. We perform calculations for the single-phase reaction with Model 1 and Model 2 at 388 and 413 K. Calculations performed with both kinetic models developed in this work show a similar trend for the 5-HMF selectivity with increasing conversion. 5-HMF selectivity is highest at very low conversions and decreases strongly above 80% conversion due to the side reactions of 5-HMF, resulting in enhanced formation of humins, LA and FA.

A difference in the initial 5-HMF selectivity for both models occurs. Model 2 starts from a theoretical selectivity of 75% and Model 1 starts from a theoretical selectivity of 100%. The reason for this difference in initial selectivity is the different description of the side reaction to humins. The coupled side reaction in Model 1 leads to a reduced humins formation at low FRC conversions as 5-HMF is limited. Model 2 with the parallel side reactions from FRC and 5-HMF predicts a significantly lower initial 5-HMF selectivity because humins can be formed directly from FRC.

LA and FA selectivity increases with increasing conversion for both models and is sensitive to reaction temperature. The general trend is an increase in LA and FA selectivity with decreasing temperature which is in good agreement to results obtained by Fachri et al. Absolute values for LA and FA selectivity obtained by Model 1 and Model 2 at 413 K (≈47% at 100% conversion) are in good agreement to reported model data at comparable conditions. Model 1 predicts a higher LA and FA selectivity at 388 K (67% at 100% conversion). Calculations performed with the kinetic model by Fachri et al at 388 K yields a LA selectivity of 65% at 99.5% FRC conversion (results not shown).

5-HMF selectivity is dependent on temperature according to calculations performed with both kinetic models. For Model 1, 5-HMF selectivity decreases with increasing temperature. This is in contrast
to results reported in previous studies. Swift et al.\textsuperscript{41} report an increasing trend in 5-HMF selectivity with increasing temperature.\textsuperscript{41} Results similar to those of Swift et al are reported by Fachri et al.\textsuperscript{10} In a recent study on 5-HMF production using a microreactor, Desir et al.\textsuperscript{42} obtain almost 54\% 5-HMF selectivity at 100\% conversion. As a result Desir et al propose high temperatures to perform efficient 5-HMF production. Selectivity of 5-HMF calculated with Model 2 slightly increases with increasing temperature, which is in good agreement to previously reported results.\textsuperscript{10,41,42}

An explanation for this different temperature sensitivity of Model 1 and Model 2 can be found by comparison of the activation energies for both models. The coupled side reaction in Model 1 has the highest activation energy of all reaction steps which results in an increased selectivity to humins at high temperatures.\textsuperscript{35} The activation energy for 5-HMF rehydration to LA and FA on the other hand is smallest, which is in agreement to Swift et al\textsuperscript{41} and Fachri et al.\textsuperscript{10} Rehydration to LA is therefore suppressed at high temperatures. However, in Model 1 the reduced rate in rehydration of 5-HMF to LA and FA is not able to compensate the increase in humins formation rate, thus resulting in an overall lower 5-HMF selectivity at high temperatures.

The structure of Model 2 is similar to already reported kinetic models.\textsuperscript{10,41} Because our obtained activation energies are also comparable (see Table 1), the reduced rate of 5-HMF rehydration to LA and FA at high temperatures is able to compensate for the higher selectivity to humins formed directly from FRC. In the case of FRC dehydra-
tation catalyzed by HCl modeled according to Swift et al.\textsuperscript{41} the reduced formation of LA and FA can even overcompensate the higher selectivity to humins, leading to higher 5-HMF yields at higher temperatures. Using H\textsubscript{2}SO\textsubscript{4} as catalyst according to Fachri et al.\textsuperscript{10} the increase of 5-HMF selectivity with increasing temperature is less pronounced.

We also attempted to integrate a further side reaction to humins in Model 1 starting only from 5-HMF to yield a more accurate description of the temperature sensitivity on 5-HMF selectivity (results not shown). However, the resulting parameters from the data regression for the parallel reaction of 5-HMF to humins had very large confidence intervals which made the obtained parameters questionable.

The differences in the 5-HMF selectivity also reflects in the overall yield, which is presented in Figure 12 for both kinetic models. The maximum yield for both kinetic models is obtained at about 70\% conversion which is in good agreement to our experimental data (see Section 4.1). At 388 K, the predicted yield of Model 1 is 40\%, thus representing our experimental data accurately. The aforementioned temperature sensitivity of the 5-HMF selectivity translates into an decreased reaction yield at 413 K calculated with Model 1.

Model 2 slightly underpredicts our experimental reaction yield with a calculated value of 36\%. As already indicated by the trends in selectivity (Figure 11), Model 2 shows increasing yields with increasing temperature. Moreover, with increasing temperature maximum yield is shifting to higher conversions. This trend is in good agreement to experimental and modeling results reported by Desir et al\textsuperscript{42} who receive almost constant selectivities over the full conversion range and therefore highest yields at full conversion.

4.4.2 Biphasic countercurrent reactor

An exemplary stationary concentration profile for the countercurrent biphasic reactor is shown in Figure 13. At the top of the reactor, the continuous phase, which consists of water, FRC, and H\textsubscript{2}SO\textsubscript{4} is introduced. FRC concentration decreases steadily until full conversion is reached at the reactor outlet. 5-HMF concentration in the aqueous phase reaches a maximum value close to the top of the reactor. This indicates that there is still a significant amount of 5-HMF in the aqueous phase present which can undergo side reactions.

The disperse phase consists of 2-MTHF and water according to the equilibrium condition at reaction temperature.\textsuperscript{13} From the bottom to the top of the reactor, 5-HMF concentration in the disperse phase is increasing due to the mass transfer from the aqueous phase. Close to the top of the reactor, 5-HMF concentration is slightly decreasing. This is due to back extraction into the continuous phase because an
almost fully loaded disperse phase contacts an empty continuous phase. This induces a change in the driving force of mass transfer and leads to back-extraction from the organic into the continuous phase.

From a comparison of the 5-HMF formation rate and the 5-HMF mass transfer rate we obtain a ratio that is significantly smaller compared to our batch experiments (see section 9 of the Supporting Information). Because the rate of 5-HMF formation is identical to the batch experiment (see Section 4.3), the smaller ratio of 5-HMF formation rate and 5-HMF mass transfer rate indicates that mass transfer limitation can be overcome in the biphasic tubular reactor. We attribute this to the much higher surface area provided by the disperse droplet phase.

To account for the effect of droplet diameter on 5-HMF yield in a technical relevant range, we provide data of a sensitivity study in section 10 of the Supporting Information. At the herein investigated reaction conditions, the increase in 5-HMF yield due to smaller droplets is less than 1%.

Selectivity for 5-HMF in the biphasic reactor is discussed as a function of conversion (Figure 14). Compared to single phase operation, the decrease in selectivity with increasing conversion is significantly lower which can be attributed to the in-situ extraction of 5-HMF. The difference in initial selectivity between calculations performed with Model 1 and Model 2 already observed in Section 4.4.1 is also present in the biphasic reactor. This can be attributed to the parallel reaction from FRC to humins in Model 2, which cannot be influenced by the in-situ extraction of 5-HMF. This drawback is already discussed by Torres et al. Model 1 with the coupled side reaction on the other hand allows the calculation of higher selectivities and hence higher 5-HMF yields.

Calculated yields for 5-HMF at different conversions in the biphasic tubular reactor are shown in Figure 15. The trend in 5-HMF yield is different from the results from the single-phase reactor (Section 4.4.1). While in the single-phase reactor the yield significantly decreases at conversions above 80%, the countercurrent biphasic reactor has a steady increase in yield to full conversion. At 388 K, 5-HMF yield is 76% based on calculations performed with Model 1 and 62% for Model 2. The difference in the maximum achievable yield for both models arises from the difference in selectivity already presented in the single-phase reaction (see Section 4.4.1).

Literature data on technical scale-production of 5-HMF in biphasic tubular reactors is rarely available. We therefore compare our modeling results with experimental results obtained in biphasic microreactors. The studies considered for comparison were all conducted in the solvent system MIBK/water using HCl as catalyst and higher temperatures than in our system. Tuercke et al report 5-HMF yields between 75 and 80% at a comparable acid concentration, a volume ratio of 3:1 (organic: aqueous) and 458 K. Lueckgen et al obtain 5-HMF yields between 83 and 93% upon operation at a higher volume ratio of 4:1 and 433 K. Shimanouchi et al report a 5-HMF yield of 73% at a volume ratio of 3:1 and 453 K.

Despite the differences in the solvent system and temperature, the results from our modeling studies conducted with Model 1 are comparable to these experimental results. The 5-HMF yield in the biphasic tubular reactor calculated with Model 2 is lower, which is due to the structure of the kinetic model. In Model 2, the formation of humins from FRC is modeled as an isolated parallel reaction, which sets a limitation to the overall 5-HMF yield.

Shimanouchi et al also differentiate between the 5-HMF yield in the MIBK phase and the total 5-HMF yield and find that almost 50% of the produced 5-HMF remains in the aqueous phase. Due to the efficient countercurrent extraction in the herein developed tubular reactor, over 99% of the produced 5-HMF is present in the organic phase (see Supporting Information). This is in good agreement to results reported by Sindermann et al for countercurrent extraction of 5-HMF on a technical scale. We believe this is a major benefit of our concept with regard to an overall 5-HMF production process. Employing the concept of a countercurrent in-situ extraction, downstream processing of the aqueous phase can be significantly simplified.
since no further separation of 5-HMF from the aqueous phase is required.

Compared to single-phase operation, LA and FA selectivity is also significantly decreased. Based on calculations with Model 1, LA and FA yield is reduced from 67 to 14% and with Model 2 from 47 to 9%. Despite the lower LA and FA yield with Model 2, the total carbon yield (calculated with Equation (6)) is lower compared to calculations performed with Model 1. The total carbon yield at 100% conversion calculated with Model 2 is 72% while calculation with Model 1 results in 90%. The lower carbon yield from Model 2 can be attributed to the higher rate of humins’ formation arising from the parallel reaction profile over the reactor height. The formation of 5-HMF in the aqueous phase and the extraction of 5-HMF into the organic phase is described by the validated reaction kinetic models developed in this work. Moreover, we consider technical scale fluid dynamics by a detailed description of the dispersed phase applying models for droplet swarm sedimentation.

From our reactor modeling study we obtain a maximum 5-HMF yield of 76% at 100% FRC conversion. A further advantage of this reactor concept is the very efficient extraction of 5-HMF (>99%) which facilitates downstream processing of the aqueous phase. Finally, the herein developed combination of experimental and model-based methods provides an innovative design framework for the technical scale-up of complex multiphase reaction systems.

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REFERENCES
1. van Putten RJ, van der Waal JC, de Jong E, Rasrendra CB, Heeres HJ, de Vries JG. Hydroxymethylfurfural, a versatile platform chemical made from renewable resources. Chem Rev. 2013;113(3):1499-1597.
2. Mukherjee A, Dumont MJ, Raghavan V. Review: sustainable production of hydroxymethylfurfural and levulinic acid: challenges and opportunities. Biomass Bioenergy. 2015;72:143-183.
3. Saha B, Abu-Omar MM. Advances in 5-hydroxymethylfurfural production from biomass in biphasic solvents. Green Chem. 2014;16(1):24-38.
4. Torres AI, Tsapatsis M, Daoutidis P. Biomass to chemicals: design of an extractive-reaction process for the production of 5-hydroxymethylfurfural. Comput Chem Eng. 2012;42:130-137.
5. Perry RH, Green DW. Perry's chemical engineers' handbook. 8th ed. New York: McGraw-Hill; 2008.
6. Shimanoouchi T, Kataoka Y, Tanifuji T, Kimura Y, Fujioka S, Terasaka K. Chemical conversion and liquid-liquid extraction of 5-hydroxymethylfurfural from fructose by slug flow microreactor. AIChE J. 2016;62(6):2135-2143.
7. Lueckgen J, Vanoye L, Philippe R, et al. Simple and selective conversion of fructose into HMF using extractive-reaction process in microreactor. J Flow Chem. 2018;8(1):3-9.
8. Hommes A, Heeres HJ, Yue J. Catalytic transformation of biomass derivatives to value-added chemicals and fuels in continuous flow microreactors. ChemCatChem. 2019;42:1357.
9. Goedecke R. Fluidverfahrenstechnik: Grundlagen, Methodik, Technik, Praxis. Vol 1. Weinheim, Germany: John Wiley & Sons; 2006.
10. Fachri BA, Abdilla RM, Bovenkamp HH, Rasrendra CB, Heeres HJ. Experimental and kinetic modeling studies on the sulfuric acid catalyzed conversion of D-fructose to 5-Hydroxymethylfurfural and Levalinic acid in water. ACS Sustain Chem Eng. 2015;3(12):3024-3034.
11. van Putten RJ, Soetedjo JNM, Pidko EA, et al. Dehydration of different ketones and aldohes to 5-hydroxymethylfurfural. ChemSusChem. 2013;6(9):1681-1687.
12. Pace V, Hoyo P, Castoldi L, Domingue de Maria P, Alcantara AR. 2-Methyltetrahydrofuran (2-MeTHF): a biomass-derived solvent with...
broad application in organic chemistry. ChemSusChem. 2012;5(8):1369-1379.

13. Glass M, Aigner M, Viell J, Jupke A, Mitsos A. Liquid-liquid equilibrium of 2-methyltetrahydrofuran/water over wide temperature range: measurements and rigorous regression. Fluid Phase Equilib. 2017;433:212-225.

14. Cadavid JG, Godoy-Silva RD, Narvaez PC, Camargo M, Fontez C. Biodiesel production in a counter-current reactive extraction column: Modelling, parametric identification and optimisation. Chem Eng J. 2013;228:717-723.

15. Minotti M, Doherty MF, Malone MF. Design for Simultaneous Reaction and Liquid–liquid extraction. Ind Eng Chem Res. 1998;37(12):4748-4755.

16. Pai RA, Doherty MF, Malone MF. Design of reactive extraction systems for bioproduct recovery. AIChE J. 2002;48(3):514-526.

17. Samant KD, Ng KM. Synthesis of extractive reaction processes. AIChE J. 1998;44(6):1363-1381.

18. Nitsch W. The concept of interfacial reactions for mass transfer in liquid/liquid systems. Faraday Discuss Chem Soc. 1984;77:85.

19. Sacher R, Nitsch W. Kopplung von Stofftransport und Grenzflächenreaktion als neuer Weg zur Kinetik der chemischen Extraktion. Chem Ing Tech. 2006;78(12):1819-1830.

20. Abdella-Santos RM, Guo W, Brujininx PCA, Yue J, Deuss PJ, Heeres HJ. High yield 5-hydroxymethylfurfural synthesis from crude sugar beet juice in a biphasic microreactor. ChemSusChem. 2019;12:4304-4312.

21. MATLAB. Version 9.6.0.1072779 (R2019a). Natick, Massachusetts: The MathWorks Inc.; 2019.

22. van Zandvoort I, Wang Y, Rasendra CB, et al. Formation, molecular structure, and morphology of humins in biomass conversion: influence of feedstock and processing conditions. ChemSusChem. 2013;6(9):1745-1758.

23. Körner P, Jung D, Kruse A. The effect of different Brønsted acids on the hydrothermal conversion of fructose to HMF. ChemSusChem. 2018;10(10):2231-2241.

24. Patil SKR, Heltzel J, Lund CRF. Comparison of structural features of humins formed catalytically from glucose, fructose, and 5-hydroxymethylfurfuraldehyde. Energy Fuel. 2012;26(8):5281-5293.

25. Kamm B. Production of platform chemicals and synthesis gas from biomass. Angew Chem Int Ed. 2007;46(27):5056-5058.

26. Szmant HH, Chundury DD. The preparation of 5-hydroxymethylfurfuraldehyde from high fructose corn syrup and other carbohydrates. J Chem Technol Biotechnol. 1981;31(1):135-145.

27. Thananathamachan T, Rauchfuss TB. Efficient route to hydroxymethylfurans from sugars via transfer hydrogenation. ChemSusChem. 2010;3(10):1139-1141.

28. Aigner M, Echtermeyer A, Kaminski S, et al. Thermodynamic modeling of a ternary system CO2/2-MTHF/water—experimental study and thermodynamic modeling. J Chem Eng Data. 2019. https://doi.org/10.1021/acs.jced.9b00315.

29. ASPEN. Aspen Plus 8.8. Aspen Tech Inc.; 1994–2019.

30. Román-Leshkov Y, Dumesic JA. Solvent effects on fructose dehydration to 5-Hydroxymethylfurfural in biphasic systems saturated with inorganic salts. Top Catal. 2009;52(3):297-303.

31. Sindermann EC, Holbach A, de Haan A, Kockmann N. Single stage and countercurrent extraction of 5-hydroxymethylfurfural from aqueous phase systems. Chem Eng J. 2016;283:251-259.

32. Henschke M. Auslegung pulsierter Siebboden-Extraktionskolonnen. Berichte aus der Verfahrenstechnik. Shaker: Aachen; 2004.

33. Richardson JF, Zaki WN. Sedimentation and fluidisation: part I. Chem Eng Res Des. 1997;75:82-100.

34. Dahmen W, Reusken A. Numerik für Ingenieure und Naturwissenschaftler. 2nd ed. Berlin, Heidelberg: Springer; 2008.

35. Levenspiel O. Chemical reaction engineering. 3rd ed. New York: John Wiley & Sons; 1999.

36. Girisuta B, Janssen LPBM, Heeres HJ. A kinetic study on the decomposition of 5-hydroxymethylfurfural into levulinic acid. Green Chem. 2006;8(8):701.

37. Mohammad S, Held C, Altunstepe E, Köse T, Sadowski G. Influence of salts on the partitioning of 5-hydroxymethylfurfural in water/MIBK. J Phys Chem B. 2016;120(16):3797-3808.

38. Weingart E, Teves L, Krieg R, Prüße U. Hexafluoropropionan as low boiling extraction solvent for 5-hydroxymethylfurfural production. Energy Technol. 2017;5(2):432-440.

39. Kalem M. Einzeltubus-Simulation von pulsierten Siebbodenkolonnen für die Reaktivextraktion. Berichte aus der Verfahrenstechnik. Shaker: Aachen; 2015.

40. Schrader B. Infrared and Raman spectroscopy. Wiley-VCH Verlag GmbH: Weinheim, Germany; 1995.

41. Swift TD, Bagía C, Choudhary V, Peklaris G, Nikolakis V, Vlachos DG. Kinetics of homogeneous Brønsted acid catalyzed fructose dehydrogenation and 5-Hydroxymethyl fufural rehydration: a combined experimental and computational study. ACS Catal. 2014;4(1):259-267.

42. Desir P, Saha B, Vlachos DG. Ultrafast flow chemistry for the acid-catalyzed conversion of fructose. Energy Environ Sci. 2019;12(8):2463-2475.

43. Tuercke T, Panic S, Loebbecke S. Microreactor process for the optimized synthesis of 5-hydroxymethylfurfural: a promising building block obtained by catalytic dehydration of fructose. Chem Eng Technol. 2009;32(11):1815-1822.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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