Enantioselective liquid-liquid extraction in microreactors
Susanti, Susanti

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2018

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
CHAPTER 2

Lactic acid extraction and mass transfer characteristics in slug flow capillary microreactor

Abstract

Capillary microreactors operated under the slug flow regime were investigated for the separation of lactic acid from the aqueous phase using liquid–liquid reactive extraction. The experiments were performed at a 1:1 flow ratio of the aqueous to organic phases in a setup consisting of an inlet Y-type mixer connected with a poly(tetrafluoroethylene) capillary microreactor and subsequently an outlet Y-shape phase splitter. The extraction of lactic acid (intake: 0.11 and 0.055 M in water) using 15% (v/v) tri-n-octylamine in 1-octanol under ambient conditions approached equilibrium after about 90 s in microreactors without noticeable emulsion formation. The measured reactive extraction performance in microreactors can be well described by a physical mass transfer model according to the penetration theory (developed from a model experimental study for the extraction of acetanilide from water to 1-octanol) combined with an instantaneous irreversible reaction assumption.
Mass transfer characteristics

2.1. Introduction

In the past a few decades, the development of microreactors in the field of chemical and process engineering has received numerous research attention. Microreactors offer a good control over process parameters due to, among others, well-defined flow pattern, efficient heat and mass transfer, fast response, and thus can be used to address the case-specific drawbacks in conventional reactors such as transport limitations (in heat or mass transfer) leading to low yields, high waste generation and cost issues related to heavy use of solvents. Advantages such as precise flow manipulation, good temperature control, enhanced safety and vast possibilities for inline measurements make microreactors attractive tools not only for chemistry and catalyst investigation on the laboratory scale, but also for chemical production on a pilot or industrial scale.

Liquid-liquid extraction, involving mass transport (in the case of physical extraction) and reaction (in the case of reactive extraction) between two immiscible liquids, is an important separation technique widely used in analytical chemistry, biology and chemical engineering. The extraction efficiency can be enhanced by maximizing the interfacial area (e.g., forming smaller droplets of the dispersed phase) and/or decreasing the mass transfer resistance. The use of microreactors for liquid-liquid extraction has shown as a promising alternative to their macroscale counterparts. This is mainly due to the significantly enhanced extraction efficiency therein since small characteristic dimension in microreactors on the micrometer scale directly translates into a high surface to volume ratio (i.e., high interfacial area available for extraction) and a low mass transfer resistance.

Up to now, many reports have been published about the exploration of microreactors for liquid-liquid extraction involving experimental and modelling studies of the process. Extraction operation including contacting two immiscible liquids, mixing and separation of both phases has been successfully demonstrated in different geometrical microreactors. Because surface forces are dominant over body forces in microreactors, phase separation by gravity is very difficult to implement. For some microreactor designs, phase separation is made relatively easy to enable almost complete separation at the microreactor outlet by means of physical supports such as membrane, guide structure and partitioned wall. Moreover, phase separation based on preferential wettability has also been explored.

Two types of common flow patterns can be discriminated when dealing with extraction using immiscible liquid phases in microchannels: parallel flow, characterized by a side-by-side flow of the immiscible fluids, and slug flow, characterized by the alternating flow of segmented fragments of the immiscible fluids. In parallel flow, mass transfer is limited...
mainly by molecular diffusion given the laminar flow nature although higher mass transfer rates can be obtained when working at higher flow rates and/or in smaller microchannels.\textsuperscript{15} A potential advantage in parallel flow operation is that the separation of the immiscible liquids at the microchannel outlet is relatively easy. Similar mass transfer performance between parallel and slug flow has been reported by Dessimoz \textit{et al.}\textsuperscript{14} for the (acid-base) neutralization reaction: the volumetric mass transfer coefficients in both flow patterns were obtained in a range of 0.2 to 0.5 s\textsuperscript{-1}. However, in contrast with parallel flow operation, slug flow operation can obtain sufficiently higher interfacial area\textsuperscript{8} and mass transfer therein is significantly enhanced by the internal circulation inside each slug or droplet.\textsuperscript{13,16}

Relatively fewer papers have been published about extraction under slug flow in microreactors compared with parallel flow. Some are related to mass transfer studies without reaction\textsuperscript{8,16–18} and some involving reactive extraction.\textsuperscript{11,14,19–21} Understanding mass transfer with reaction during extraction under slug flow in microreactors is not trivial given the somewhat complex nature of slug flow. The published work so far is mostly concerned with empirical descriptions without physically sufficient reasoning. Therefore, an in-depth experimental and theoretical study of reactive extraction under slug flow in microreactors is necessary.

This work presents an experimental investigation into reactive liquid-liquid reactive extraction in microreactors involving the extraction of lactic acid from the aqueous phase with tri-n-octylamine (TOA) as an extractant in 1-octanol as diluent. Lactic acid is an important bio-based chemical used for the commercial production of polylactic acid (a bio-based and biodegradable plastic) and is currently produced by the fermentation of glucose or other six-carbon sugars (e.g., disaccharides like sucrose or lactose).\textsuperscript{22–26} However, conventional lactic acid isolation from fermentation broth has some major drawbacks, for example, in the use of large amount of alkali (i.e., lime) and relatively expensive sulfuric acid, the production of large amounts of solid waste (i.e., calcium sulfate) and involving multistep purification.\textsuperscript{23,27,28} Thus, liquid-liquid reactive extraction has been proposed as an attractive alternative to circumvent these issues for the isolation of lactic acid.\textsuperscript{23}

Several developments are needed to bring lactic acid recovery by reactive extraction to an industrially competitive level. Interesting developments have taken place in the selection and design of the extractant and diluents for lactic acid recovery recently.\textsuperscript{29–34} Process intensification using microreactors could be applied under normal or especially extreme conditions (e.g. at elevated pressure and temperature) to explore more efficient extractive recovery regimes.\textsuperscript{35,36} The traditional TOA in 1-octanol system as used in this work is suitable as a model solvent system for investigating fundamentals into mass transfer with chemical reaction
in such reactive extraction. Moreover, amine extractants such as TOA have a promising performance for the separation of carboxylic acid from the aqueous phase.²⁴,³⁷ Beside good capacity, high concentration of TOA exhibits low toxicity to *Lactobacillus delbrueckii* (i.e., one of the microorganisms in fermentation process).³⁷ Therefore, reactive extraction using TOA in 1-octanol combined with slug flow operation in microreactors is expected to hold great promises for developing an alternative technology for lactic acid isolation from fermentation broths.

The main objective of this work is to gain insight in mass transfer characteristics of slug flow operated capillary microreactors with a non-chiral reactive extraction system, i.e. lactic acid extraction from an aqueous phase using tri-octylamine (TOA) as the extractant in 1-octanol. Included are also physical extraction studies of acetanilide from a water phase to an organic phase (1-octanol) to obtain relevant mass transfer data. Both reactive extraction and physical extraction under slug flow operation has been experimentally studied in a capillary microreactor at different residence times. The influence of the residence time on mass transfer was investigated by varying the total flow rate and/or length of the capillary microreactors.

### 2.2. Experimental details

#### 2.2.1. Materials

Briliant Blue FCF, Sudan III, acetanilide (≥ 99.5%), lactic acid (85%) and n-octanol (≥ 99%) were obtained from Sigma Aldrich. Tri-n-octylamine was obtained from Across-organic. Two syringe pumps (model No. LA30, HLL Gmbh) were used for fluid delivery. Poly(tetrafluoroethylene) (PTFE) tubings (BOLA) were used as capillary microreactors. The imaging system consists of a digital camera (model powershot SX220 HS, Canon).

#### 2.2.1. Experimental setup

A schematic experimental setup is shown in Figure 2.1. The aqueous and organic phases were delivered by two syringe pumps and were introduced to a homemade 120°-angled Y-shape inlet mixer [1 mm inner diameter; made of (poly)methyl methacrylate] that was connected to a PTFE capillary microreactor of different lengths (1.6 mm outer diameter and 0.8 mm inner diameter) of different lengths. The two phases were separated at the end of the capillary microreactor using a home-made Y-shape splitter which consisted of a PTFE tube and a glass tube of the same dimension (i.e., 1.6 mm outer diameter and 0.8 mm inner diameter) that were inserted into the splitter block. The separation in the splitter was based on the preferential wettablity difference: the aqueous phase
Chapter 2

has strong affinity towards glass whereas the organic phase has affinity towards PTFE. The aqueous phase from the glass outlet was collected and analyzed.

2.2.2. Experimental procedures
To investigate the liquid-liquid extraction and mass transfer characteristics in the microreactors, both physical and reactive extraction experiments were performed. All experiments were performed at ambient conditions (ca. 0.1 MPa, 25°C). The physical properties of the solvents used are given in Table 2.1, as found from the literature.38

<table>
<thead>
<tr>
<th>Liquid</th>
<th>Density [kg/m³]</th>
<th>Viscosity [Pa·s]</th>
<th>Surface tension with water [N/m]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>998</td>
<td>1×10⁻³</td>
<td>–</td>
</tr>
<tr>
<td>n-octanol</td>
<td>822</td>
<td>7.3×10⁻³</td>
<td>8.19×10⁻³</td>
</tr>
</tbody>
</table>

The partition coefficient and diffusivity of chemicals used in both phases are shown in Table 2.2. The partition coefficient \( m \) was determined
from our experimental measurements: the experiments were performed in small glass vials of 20 mL, where 5 mL of the aqueous phase (i.e., containing acetanilide or lactic acid at various concentrations) was mixed with 5 mL 1-octanol. The phases were stirred at 500 rpm for 18 h, then allowed to settle for 2 h; the aqueous phase was separated and analyzed (vide infra). Then, \( m \) could be calculated as

\[
m = \frac{C_{\text{org,eq}}}{C_{\text{aq,eq}}} \tag{2.1}
\]

Where \( C_{\text{org,eq}} \) and \( C_{\text{aq,eq}} \) are the equilibrium concentrations of the solute (i.e., acetanilide or lactic acid) in the organic and aqueous phases when only physical extraction takes place, respectively. The diffusivity of chemicals \( (D) \) used in both phases are either obtained from the literature or based on an approximation according to the Stokes-Einstein equation:\(^{39}\)

\[
\frac{D \mu}{T} = \text{constant} \tag{2.2}
\]

### 2.2.3.1. Physical extraction

To characterize mass transfer without reaction in the capillary microreactors, physical extraction experiments were performed using the water/1-octanol system, with acetanilide as the mass transfer component (its initial aqueous concentration being 1.5 mM or 0.81 mM). Pure 1-octanol was used as the organic phase at the microreactor inlet. Extraction was carried out at several capillary microreactor lengths and flow rates (i.e., at varying residence times) with the flow ratio of the aqueous to organic phase being kept constant at 1:1. For slug flow operation, the residence time \( (\tau) \) is calculated by Eq. 2.3.
\[ \tau = \frac{V_c}{Q_{aq} + Q_{org}} = \frac{\pi d_c^2 L_c}{4 (Q_{aq} + Q_{org})} \]  

(2.3)

where \( V_c, d_c, \) and \( L_c \) are the volume, inner diameter and length of the capillary microreactor, respectively. \( Q_{aq} \) and \( Q_{org} \) are the flow rates of the aqueous and organic phases, respectively. The volumetric flow rate of each phase was varied between 2.5 and 12.5 mL/h.

### 2.2.3.2. Reactive extraction

The characteristics of reactive extraction in the capillary microreactors were investigated for lactic acid extraction with TOA. Lactic acid dissolved in water as the aqueous phase was extracted by TOA in 1-octanol as the organic phase. TOA [15% (V/V)] in 1-octanol was used for two typical initial concentrations of lactic acid in the aqueous phase (i.e., 0.11 M and 0.055 M) based on the optimum extraction efficiency observed from the equilibrium study in our batch experiments: the batch experiments were performed in small glass vials of 20 mL, where 5 mL of 0.11 M lactic acid in water was mixed with 5 mL 1-octanol containing various amount of TOA [ranging from 5-40% (V/V)]; the two phases were stirred at 500 rpm for 18 h, then allowed to settle for 2 h; the aqueous phase was separated and analyzed (\textit{vide infra}).

The influence of the residence time was investigated by following the same procedure as that used in the physical study (i.e., by changing the microreactor length and flow rate of each phase was varied between 2.5 and 12.5 mL/h; the aqueous to organic phase was 1:1).

### 2.2.3.3. Slug flow pattern visualization

The use of equal flow rate between the aqueous and organic phases through an inlet 120° angled Y-shape inlet mixer generated a stable slug flow in the subsequent capillary microreactor. For the purpose of visualizing the slug flow pattern (e.g., to enable the slug and droplet size measurement), Brilliant Blue FCF dye was added into the aqueous phase in additional physical extraction experiments, and SUDAN III dye was added into the organic phase in additional reactive extraction experiments (with the concentration of each dye being 0.3 mM), while the other operational conditions being unchanged. Note that the extraction performance was evaluated in the respective experiments in the absence of dyes. The slug flow pattern visualization in the capillary microreactors was made by camera-snapshots (model Powershot SX220 HS, Canon) and repeated at least twice to ensure a good reproducibility.
2.2.3.4. Analytical procedures
The concentration of the solute in the aqueous phase was analyzed by a TIDAS UV−vis spectrophotometer (type RS 422, J&M Analytische mess- and Regeltechnik GmBH) at λ = 250 and 210 nm for acetanilide and lactic acid, respectively. The concentration of acetanilide or lactic acid (in all forms) in the organic phase was calculated according to the mass balance. All data provided are the averages from multiple experiments that showed good reproducibility.

2.3. Results and discussion

2.3.1. Mass transfer in physical extraction
The physical extraction behavior of the microreactor system under slug flow operation was studied using a model system, being the extraction of acetanilide from water to 1-octanol. The extraction efficiency and overall physical volumetric mass transfer coefficient were evaluated.

The extraction efficiency (η), defined as the ratio between the amount of material transferred from one phase to the other and the maximum transferable amount, is determined for the current physical extraction system according to the following equation:

\[ \eta = \frac{C_{aq,0} - C_{aq,1}}{C_{aq,0} - C_{aq,eq}} \times 100\% \]  (2.4)

where \( C_{aq,0} \) and \( C_{aq,1} \) are the concentrations of the solute (i.e., acetanilide in this case) in the aqueous phase at the microreactor inlet and outlet, respectively. \( C_{aq,eq} \) represents the concentration of the solute in the aqueous phase when physical extraction reaches equilibrium.

The extraction efficiency for the extraction of acetanilide from its aqueous solution into 1-octanol as a function of the residence time (\( \tau \)) in the present 0.8 mm diameter capillary microreactors is shown in Figure 2.2. The extraction efficiency increases with an increase in the residence time, approaching 100% after around 60 s. This indicates a fast extraction process primarily due to the enhanced physical mass transfer rates in the microreactor. At the same residence time, the use of different inlet concentrations of acetanilide in the aqueous phase (i.e., 1.5 mM and 0.81 mM) gave the same extraction efficiency. This implies that under the investigated conditions, the extraction efficiency is independent of the inlet concentration of acetanilide and is only dependent on the residence time (see Appendix 2A).

The overall physical volumetric mass transfer coefficient, \((K_{v,a})_{phys}\), is a characteristic parameter used to evaluate the performance of liquid-liquid
conducting a mass balance. Then, it is obtained that

\[ (K_{ov,a})_{PHYS} = \frac{Q_{aq} \left( C_{aq,0} - C_{aq,1} \right)}{V_c \Delta C_m} \] (2.5)

where the mean concentration difference is defined as

\[ \Delta C_m = \left( \frac{C_{aq,1} - C_{org,1}}{m} \right) - \left( \frac{C_{aq,0} - C_{org,0}}{m} \right) \int \frac{C_{aq,1} - \frac{C_{org,1}}{m}}{C_{aq,0} - \frac{C_{org,0}}{m}} \] (2.6)

Here \( C_{org,0} \) and \( C_{org,1} \) are the concentrations of the solute (i.e., acetanilide) in the organic phase at the microreactor inlet and outlet, respectively. As pure 1-octanol was used at the inlet, \( C_{org,0} = 0 \). Eq. 2.5 represents an averaged calculation of \( (K_{ov,a})_{PHYS} \) in the present physical extraction.
experiments assuming plug flow behavior and no radial concentration gradient in the bulk of each phase, which is commonly accepted for engineering calculations without the necessity of knowing the underlying hydrodynamics and mass transfer details.

Figure 2.3a show the measured \( (K_{oa})_{phys} \) values in the capillary microreactors versus the microreactor length at different residence times. Here, the residence time was kept constant by varying the microreactor length and the total flow rate (cf. Eq. 2.3). The important observation is no difference in the \( (K_{oa})_{phys} \) values for the same residence time. Another observation, the \( (K_{oa})_{phys} \) values higher at shorter residence times. This is further verified in Figure 2.3b in which the measured \( (K_{oa})_{phys} \) values are plotted with the variation in the phasic flow rate (the aqueous-organic flow ratio being 1:1). For a given microreactor length, \( (K_{oa})_{phys} \) value is
higher at a higher total flow rate (i.e., at a shorter residence time). In other words, the variations in the total flow rate and the microreactor length have no impact on \( (K_{ov,\text{phys}}) \) as long as the residence time is the same. At a given phasic flow rate combination, \((K_{ov,\text{phys}})\) value along the capillary length is seen to decrease. This clearly suggests that the measured \((K_{ov,\text{phys}})\) value is mainly a function of the residence time in the present experiments.

The measured \((K_{ov,\text{phys}})\) value as a function of the residence time is further depicted in Figure 2.4, which is well described by the following relationship:

\[
(K_{ov,\text{phys}}) = \frac{0.214}{\sqrt{\tau}}
\]  

(2.7)

Here, \((K_{ov,\text{phys}})\) is in \(s^{-1}\) and \(\tau\) in s. Since the aqueous-organic flow ratio was 1:1 in all our experiments, the specific interfacial area \((a)\) is practically the same for all operational conditions (as will be shown hereafter). Thus, it indicates that the overall physical mass transfer coefficient, \((K_{ov,\text{phys}})\) is generally inversely proportional to \(\sqrt{\tau}\), which is in agreement with the Higbie’s penetration theory.44 In the present work, all the measured \((K_{ov,\text{phys}})\) values (in 0.8 mm diameter capillary microreactors) are in a range of 0.03-0.09 \(s^{-1}\), which are comparable with the values reported by Kashid et al.8 (i.e., 0.02-0.32 \(s^{-1}\) for the extraction of succinic acid in the aqueous phase with n-butanol in capillary microreactors having diameters

---

**Figure 2.4.** Overall physical volumetric mass transfer coefficient for physical extraction of acetanilide with 1-octanol in 0.8 mm capillary microreactors. Solid line represents fitting of the experimental data with Eq. 2.7.
Mass transfer characteristics

Figure 2.3 also shows that \((K_{ov})_{phys}\) is independent of the inlet acetanilide concentration in the aqueous phase (i.e., 1.5 mM and 0.81 mM), which confirms the correctness of our experimental methods. The agreement between the experimental measurements and the Higbie’s penetration theory as observed above has led us to formulate a simple model to describe the underlying mass transfer behavior during physical extraction in the investigated capillary microreactors. It is envisaged that the extraction of acetanilide from the aqueous phase to the organic phase under slug flow operation in the microreactor took place via the following mass transfer steps (Figure 2.5)\(^{45,46}\): (1) transfer of acetanilide from the bulk of the aqueous droplet (i.e., the droplet center) to the aqueous-organic interface; (2) transfer of acetanilide from the interface to the bulk of the organic slug (i.e., the slug center); (3) transfer of acetanilide from the aqueous-organic interface to the organic film surrounding the aqueous droplet; (4) mixing of acetanilide between the organic film and the organic slug. Furthermore, mass transfer steps (1), (2), and (4) are facilitated by inner recirculation in the droplet and liquid slugs (cf. Figure 2.5b)\(^8,21,47\).

In the present study, we simply assume that mass transfer steps 3 and 4 may be accounted for by a combination with mass transfer step 2. That is, no differentiation is made between the organic slug and the organic film.
and thus the entire interface will be used for mass transfer calculation in step 2. It is known that mass transfer into a quiescent liquid is described by the Higbie’s penetration theory at small Fourier numbers (typically < 0.1). If we neglect the inner recirculation in both the aqueous droplet and the organic slug, we can consider them both as stagnant fluids (i.e., in a reference frame with the microreactor wall moving at the droplet speed) and can thus define a characteristic Fourier number for each phase as

\[
F_{O_{org}} = \frac{D_{org} \tau}{\left( \frac{L_{org}}{2} \right)^2} \quad (2.8)
\]

\[
F_{O_{aq}} = \frac{D_{aq} \tau}{\left( \frac{L_{droplet}}{2} \right)^2} \quad (2.9)
\]

where \( D_{org} \) and \( D_{aq} \) denote the diffusivities of the solute (i.e., acetanilide in this case) in the organic and aqueous phase, respectively. For all physical extraction experiments, the calculated ranges from \(3.6 \times 10^{-4}\) to \(8.6 \times 10^{-3}\) and from \(2.3 \times 10^{-3}\) to \(4.9 \times 10^{-2}\). Given such small Fourier numbers, the local physical mass transfer coefficient in each phase (i.e., \( k_{L_{org}} \) and \( k_{L_{aq}} \)) can be determined according to the penetration theory as

\[
k_{L_{org}} = 2 \sqrt{\frac{D_{org}}{\pi \tau}} \quad (2.10)
\]

\[
k_{L_{aq}} = 2 \sqrt{\frac{D_{aq}}{\pi \tau}} \quad (2.11)
\]

Then, the overall physical mass transfer coefficient, \((K_{ov})_{phys}\) is derived as

\[
(K_{ov})_{phys} = \frac{1}{\frac{1}{k_{L_{aq}}} + \frac{1}{mk_{L_{org}}}} \quad (2.12)
\]

and thus the overall physical volumetric mass transfer coefficient is found as
\[
(K_{ov,a})_{phys} = \left(\frac{1}{2 \sqrt{\frac{D_{aq}}{\pi \tau}} + \frac{1}{2m \sqrt{\frac{D_{org}}{\pi \tau}}}}\right) a
\]  

(2.13)

Here \(a\) represents the entire interfacial area available for mass transfer including the organic film region and slug region since the film contribution in mass transfer (i.e., mass transfer steps 3 and 4 as specified above) has been combined with the slug contribution. In the literature, it has been seen that considering the film region is important to determine the interfacial area in slug flow since the presence of the film gives a substantial rise in \(a\) for a long droplet,\(^{47}\) and including the film gives much better agreement between modeling study and the experimental results.\(^{8}\)

With the presence of an organic film, the interfacial area is determined by

\[
a = \frac{\pi d_{droplet}^2 + \pi d_{droplet} L_{film}}{\frac{1}{4} \pi d_c^2 (L_{droplet} + L_{slug})}
\]  

(2.14)

where \(L_{droplet}, L_{film},\) and \(L_{slug}\) represent the lengths of the aqueous droplet, organic film and organic slug, respectively (cf. Figure 2.5a). In this work, the measured droplet and slug lengths were found to be almost the same at all conditions with deviation less than 5% (i.e., \(L_{droplet} L_{slug} A d_c\)), which is reasonable as the current experiments were carried out at an aqueous to organic flow ratio at 1:1. In Eq. 2.14, \(d_{droplet}\) is the diameter of the aqueous droplet end caps that are approximated as hemi-spherical and is assumed to be as almost equal to the capillary microreactor diameter (i.e., \(d_{droplet}, d_c\)) based on the fact that the liquid film thickness is very thin under the present conditions give low capillary numbers involved \((C_a = 2.4 \times 10^{-3} - 1.2 \times 10^{-2})\).\(^{47,49}\) Here, \(Ca\) is the capillary number calculated as

\[
Ca = \frac{\mu_{org}(j_{aq} + j_{org})}{\sigma}
\]  

(2.15)

where \(\mu_{or}\) is the viscosity of the organic phase, \(j_{aq}\) and \(j_{org}\) are the superficial velocities of the aqueous and organic phases, respectively, and \(\sigma\) is the surface tension between the aqueous and organic phases. Furthermore, \(L_{film}\) can be calculated using the following relationship:
\[ L_{film} = L_{droplet} - d_c \]  

(2.16)

Under all the present experimental conditions, the calculated interfacial area ranges from 2640 to 2730 m²/m³, which is comparable with the reported values for extraction of iodine with kerosene under slug flow operation in capillary microreactors of similar diameters.⁸

Therefore, the overall physical volumetric mass transfer coefficient, \((K_{ov,a})_{phys}\), can be finally rearranged as

\[
(K_{ov,a})_{phys} = \left( \frac{1}{\frac{1}{2D_{aq}} + \frac{1}{2mD_{org}}} \right) \left( \frac{3d_c + L_{droplet}}{d_c(L_{droplet} + L_{slug})} \right)
\]

(2.17)

The calculated \((K_{ov,a})_{phys}\) value based on the developed model (i.e., Eq. 2.17) is compared with the measured \((K_{ov,a})_{phys}\) value in our experiments in Figure 2.6. The measured \((K_{ov,a})_{phys}\) values are consistently about 2.6 times the model predictions. The underestimation in the model predictions can be explained primarily by the fact that not only molecular diffusion contributes to mass transfer in slug flow, but also the inner recirculation present in both the aqueous droplet and the organic slug enhances only molecular diffusion contributes to mass transfer in slug flow, but also the inner recirculation present in both the aqueous droplet and the organic slug enhances only molecular diffusion contributes to mass transfer in slug flow, but also the inner recirculation present in both the aqueous droplet and the organic slug enhances only molecular diffusion contributes to mass transfer in slug flow, but also the inner recirculation present in both the aqueous droplet and the organic slug enhances

\[ C_{aq0} = 1.5 \text{ mM} \]
\[ C_{aq0} = 0.81 \text{ mM} \]

**Figure 2.6.** Comparison between the measured overall physical volumetric mass transfer coefficients for physical extraction of acetaldehyde in 0.8 mm capillary microreactors and model predictions with Eq. 2.17. Solid line represents the linear correlation with a slope of 2.6.
recirculation present in both the aqueous droplet and the organic slug enhances significantly interfacial mass transfer via convective diffusion (cf. Figure 2.5b).

Then, the developed physical mass transfer model can be further refined as

$$K_{vo, a}_{phys} = 2.6 \left( \frac{1}{2} \frac{D_{aq}}{\pi \tau} + \frac{1}{2m} \frac{D_{org}}{\pi \tau} \right) \left( \frac{3d_c + L_{droplet}}{d_c \left( L_{droplet} + L_{slug} \right)} \right)$$

(2.18)

A constant of 2.6 as found here suggests that the enhancement of inner recirculation in slug flow on an otherwise molecular diffusion-dominant mass transfer is not (or less) dependent on the phasic flow rate under the current experimental conditions at 1:1 aqueous to organic flow ratio, which can be qualitatively analyzed by considering the concentration field inside the liquid slug and the droplet.

In the liquid slug, two counter-rotating vortices appear in a coordinate moving at the droplet speed, with closed streamlines and a pattern symmetrical about the center axis (cf. Figure 2.5b).50,51 Within each vortex, convective transport of the solute takes place along the rotation direction while the dominant molecular transport is perpendicular to the rotation direction (described by the penetration theory given small Fourier numbers), affording the lowest solute concentration in the center region of each vortex (e.g., see Figure 3 in a recent simulation work by Zhang et al.52 for a typical concentration field under liquid-liquid slug flow mass transfer in microreactors). If the recirculation is simply assumed to be extremely fast, one would imagine that the interfacial concentration is immediately built up at the outer boundary of each vortex (i.e., the circumference of the liquid slug and the center plane in a three-dimensional view, besides the interface at the slug end). Thus, the enhancement of internal recirculation in the liquid slug on mass transfer may be understood practically by the creation of additional “fictitious interface area” available for mass transfer (i.e., the interfacial area of the liquid slug and that of the center plane). A similar analysis can be done for mass transfer enhancement in the droplet, where the additional “fictitious interface area” is the interfacial area of the liquid film and that of the center plane within the droplet (cf. Figure 2.5b).

In our experimental study, the liquid slug and droplet lengths were almost equal due to the 1:1 flow ratio employed. Then, the presence of internal recirculation in both the liquid slug and the droplet tends to yield an increase of $(K_{vo, a})_{phys}$ by a factor of about 2 or slight higher than 2 as
compared with the model prediction using Eq. 2.17 (i.e., the “fictitious interface area” is nearly the same for both the liquid slug and the droplet and is roughly equal to or slighter higher than \(a\) as specified by Eq. 2.14 or as further elaborated in Eq. 2.17). The obtained constant of 2.6 in our experiments (cf. Figure 2.6) is in qualitative agreement with this estimation. Based on the above analysis, it is expected that the value of this constant may vary depending on the length ratio between the liquid slug and the droplet (or equivalently the aqueous-organic flow ratio).

However, it must be admitted that the above analysis is highly idealized and simplified without in-depth consideration of local slug flow hydrodynamics and mass transfer. A more elaborate analysis and fundamental insights into the enhancement of internal recirculation will be further sought in our ongoing numerical mass transfer study. The numerical work will allow to reveal in great detail how the internal recirculation affects the concentration field and mass transfer rate, and how the film contribution in mass transfer interacts precisely with the slug contribution.

With the refined mass transfer model (i.e., Eq. 2.18), the observed independence of the extraction efficiency on the inlet aqueous acetanilide concentration in the present experiments as shown in Figure 2.2 can be well explained (Appendix 2A).

### 2.3.2. Mass transfer in reactive extraction

Mass transfer investigation in reactive extraction involved the extraction of 0.11 M or 0.055 M lactic acid from its aqueous phase with 15% (V/V) TOA (0.34 M) in 1-octanol in the above-mentioned capillary microreactors. Lactic acid is a weak acid and dissociates in the aqueous phase according to

\[
\text{LA} + \text{H}^+ \rightleftharpoons \text{LA}^- + \text{H}^+, \tag{2.19}
\]

where \(\text{LA}\) and \(\text{LA}^-\) represents the free and dissociated forms of lactic acid in the aqueous phase, respectively. The dissociation constant \((K_a)\) is \(1.38 \times 10^{-4}\) at 25°C.\(^5\)\(^3\) The extent of lactic acid dissociation is found not very significant in our study, for the concentration intake of 0.11 M and 0.055 M lactic acid, the average percentage of the dissociated form throughout the microreactor is below around 11% (Appendix 2B). Thus, for a first approximation, we may neglect the dissociated form and the formation of complexes between lactic acid and TOA can be described by a simple additive model consisting of the following steps:\(^4\)\(^0\)
Mass transfer characteristics

\[
[R_3N] + \text{LA} \rightleftharpoons [R_3N\cdot\text{LA}] \quad (2.20a)
\]

\[
[R_3N\cdot\text{LA}] + \text{LA} \rightleftharpoons [R_3N\cdot(\text{LA})_2] \quad (2.20b)
\]

\[
[R_3N\cdot\text{LA}] + [R_3N] \rightleftharpoons [(R_3N)_2\cdot\text{LA}] \quad (2.20c)
\]

where \(R_3N\) represent TOA and free lactic acid, respectively, with species in the organic phases marked with square bracket. \(K_{11}, K_{21}, \) and \(K_{12}\) are the equilibrium constants for the formation reaction of 1:1, 2:1 and 1:2 lactic acid-TOA complexes, respectively. Along with the formation of complexes, an equilibrium is also established between free lactic acid in both phases. In the current reactive extraction experiments, TOA was in excess and thus the complexes were assumed to exist predominantly in the 1:1 form (cf. Eq. 2.20a), which is supported by the fact that \(K_{11}\) is much larger than \(K_{21}\) and \(K_{12}\) at the investigated conditions (see Table 2 in the work of Qin et al.\textsuperscript{40}).

It is known that the isolation of lactic acid using liquid-liquid reactive extraction has a tendency to form emulsion, for example, in conventional reactors under high-shear turbulent mixing or in hollow fiber membrane extraction process.\textsuperscript{23} In such cases, the generated droplet size can be well below 100 μm leading to emulsion formation.\textsuperscript{54} In our microreactors, there is an absence of turbulent mixing due to laminar flow nature, thus very small droplets could not be generated. Moreover, the droplets were expected to be generated at the Y-shape inlet mixer in the squeezing regime given low capillary numbers, where the forces involved in the droplet break-up process include the surface tension force, the shear force exerted by the continuous phase, and the force arising from pressure drop across the emerging droplet (which is the dominant force in the break-up dynamics).\textsuperscript{55} The size of thus generated droplets was reproducible and several times the microreactor diameter under the investigated conditions (i.e., \(L_{\text{droplet}} \approx 4d_c = 3.2\) cm). Hence, emulsions were not observed in the current capillary microreactors during the extraction of lactic acid with 15% (V/V) TOA in 1-octanol. This ensures an easy separation of both the aqueous and organic phases based on the preferential wettability at the end of the capillary microreactors using the homemade Y-shape splitter (cf. Figure 2.1).

Reactive extraction in the current capillary microreactors was performed at different residence time values (\(\tau\)) and the corresponding extraction efficiency as a function of the residence time was plotted in Figure 2.7. Note that the extraction efficiency here was calculated using Eq. 2.4, in which \(C_{\text{aq,0}}\) and \(C_{\text{aq,1}}\) are the concentrations of the solute
Chapter 2

(i.e., lactic acid in this case) in the aqueous phase at the microreactor inlet and outlet, respectively, and $C_{aq,eq}$ represents the concentration of the solute in the aqueous phase when the reactive extraction reaches equilibrium obtained from our additional experiments in batch reactors (Appendix 2C). Figure 2.7 reveals that compared with physical extraction case, the extraction efficiency in reactive extraction is dependent on not only the residence time, but also the inlet lactic acid concentration in the aqueous phase. The lower the inlet lactic acid concentration, the higher the extraction efficiency. This trend is more obvious at short residence times at which the extraction is far from equilibrium. The observed dependence here is further explained in details in Appendix 2C. The equilibrium seems to be approached at a residence time above 90 s in the investigated microreactors, which is considerably faster compared with our additional experiments in a small vial in batch mode (i.e., 5 mL organic phase was placed as a layer on top of a 5 mL aqueous phase layer; TOA and lactic acid concentrations were kept unchanged; only the aqueous phase was stirred at a rate of 500 rpm in order not to distort the clear aqueous-organic interface). In this batch study, it took almost 1 h to reach equilibrium. Reactive extraction of several carboxylic acids using TOA at high speed of mixing rate was demonstrated by Rasrendra et al.\textsuperscript{56} It involved the continuous reactive extraction in a centrifugal contactor separator, a device basically consisting of a rotating centrifuge in a static housing that combines efficient mixing and fast separation of two immiscible liquids. At a rotation speed of 3000 rpm, the extraction reached equilibrium after 15 min.\textsuperscript{56} This comparison suggests that mass transfer in microreactors

![Figure 2.7](image-url)
is significantly enhanced along with a fast-intrinsic complexation rate between lactic acid and TOA.

To explain the observed extraction performance, a mass balance analysis for the extracted lactic acid from the aqueous phase to the organic phase was first performed over an elementary volume of the capillary microreactor as follows:

\[ Q_{\text{org}} dC_{\text{org}} = -Q_{\text{aq}} dC_{\text{aq}} = (K_{e,a})_{\text{chem}} \left( C_{\text{aq}} - \frac{C_{\text{org}}}{m} \right) dV_c \]  \hspace{1cm} (2.21)

Here \( C_{\text{aq}} \) and \( C_{\text{org}} \) are the bulk concentration (i.e., the average concentration) of free lactic acid in the aqueous and organic phases, respectively. \((K_{e,a})_{\text{chem}}\) represents the overall chemical volumetric mass transfer coefficient in reactive extraction that further takes into account of the enhancement of chemical reaction on the extraction rate.

Kinetics for lactic acid complexation with amine compounds in several diluents has been reported by Wasewar et al.\(^{57}\) The reaction rate constant for the forward reaction of lactic acid with alamine-336 in 1-octanol was found as 24 s\(^{-1}\) (zero order in alamine-336; first order in lactic acid) and it is a relatively fast reaction.\(^{57}\) It has been known that alamine-336 is a mixture of straight-chain tertiary amines with 8-10 carbon atoms.\(^{58}\) Therefore, TOA as a pure tertiary amine with 8 carbon atoms, for a first approximation, is assumed to react with lactic acid in 1-octanol instantaneously in the current microreactors under the investigated experimental conditions although the exact kinetic data for this system are not available yet. As such, this approximation neglects the reversible nature of the complexation (cf. Eq. 2.20), which is based on the fact that the equilibrium, if approached, only took place towards the outlet of the present microreactors (viz. a large portion of the microreactor was still far from equilibrium).

By assuming the presence of an irreversible instantaneous reaction regime, it is obtained that

\[ C_{\text{org}} = 0 \]  \hspace{1cm} (2.22)

This means that the free form of lactic acid is not present in the bulk of the organic phase. Eq. 2.22 is also based on the fact that in our experiments, TOA was never depleted at the microreactor outlet (i.e., the abundant TOA was assumed to bind any lactic acid transferred organic phase to predominantly form 1:1 complexes). If we represent the current reactive extraction in slug flow in a simplified view according to the two-film
theory (as shown in Figure 2.8), mass transfer is assumed to take place inside a thin film region in each phase adjacent to the interface. Inside the film region on the organic side, lactic acid meets with TOA at the reaction plane and reacts instantaneously there. In this simplified irreversible reaction model, as long as free TOA is available in the organic phase, free lactic acid does not exist in the bulk therein.

Then, Eq. 2.21 can be reduced to

$$-Q_{aq}dC_{aq} = (K_{aq,a})_{Chem} C_{aq} dV_c$$  \hspace{1cm} (2.23)

Integration throughout the capillary microreactor leads to

$$(K_{aq,a})_{Chem} = \frac{Q_{aq}}{V_c} \ln \frac{C_{aq,0}}{C_{aq,1}}$$  \hspace{1cm} (2.24)$$
Figure 2.9 shows the experimentally measured (\(K_{ov,a}\))\text{Chem} value according to Eq. 2.24 versus the residence time for reactive extraction of lactic acid at two different inlet concentrations in the microreactors (i.e., 0.11 M and 0.055 M). A similar trend to that in physical extraction experiments was observed: the measured (\(K_{ov,a}\))\text{Chem} value increases with decreasing residence time and seems to be a function of the residence time regardless of the investigated flow rate or microreactor length. This implies the existence of a direct relation between the overall volumetric mass transfer coefficients obtained from physical and reactive extraction experiments. However, unlike in the case of physical extraction, the measured (\(K_{ov,a}\))\text{Chem} value that takes into account of the enhancement of chemical reaction depends on the inlet lactic acid concentration as well: (\(K_{ov,a}\))\text{Chem} value is higher at lower inlet lactic acid concentration, which is more obvious at short residence times (e.g., < 60 s); at long residence times, (\(K_{ov,a}\))\text{Chem} does not differ much for both inlet concentrations (Appendix 2D).

From the investigated physical extraction experiments, it has been found that the overall physical volumetric mass transfer coefficient, (\(K_{ov,a}\))\text{Chem}, is well represented by Eq. 2.18. Given the small Fourier numbers in the current reactive extraction experiments (\(Fo_{org}\) ranging from \(5 \times 10^{-4}\) to \(6.8 \times 10^{-3}\) and \(Fo_{aq}\) from \(3.5 \times 10^{-3}\) to \(6 \times 10^{-2}\); calculated using eqs. 2.8 and 2.9 in which \(D_{org}\) and \(D_{aq}\) denote the diffusivities of lactic acid in the organic and aqueous phases, respectively) and other similar flow conditions (i.e., the aqueous-organic flow ratio at 1:1), the criterion to derive Eq. 2.18 is
also applicable here. Thus, according to the mass transfer scenario shown in Figure 2.8, it is reasonable to arrive at:

\[
(K_{ov}a)_{Chem} = 2.6 \left( \frac{1}{1 + \frac{1}{2} \left( \frac{D_{aq}}{\pi \tau} + \frac{D_{org}}{\pi \tau} \right)} \right) \left( \frac{4L_{droplet}}{d_i (L_{droplet} + L_{slug})} \right) \tag{2.25}
\]

where \( E_i \) is the instantaneous enhancement factor according to the two-film theory represented as\(^60\)

\[
E_i = 1 + \frac{D_{TOA} C_{TOA}}{z D_{org} C_{org}} \tag{2.26}
\]

where \( C_{org}^* \) and \( C_{TOA} \) denote the interfacial concentration of free lactic acid and the bulk concentration of TOA on the organic phase side (cf. Figure 2.8b), respectively. \( z \) is the stoichiometric ratio between lactic acid and TOA, which is approximated as 1 here due to the assumption of the predominant formation of 1:1 complexes (cf. Eq. 2.20a). \( D_{TOA} \) is the diffusivity of TOA in the organic phase (1-octanol), which is almost equal to that of lactic acid (i.e., \( D_{TOA} \approx D_{org} \); cf. 0). Hence, Eq. 2.26 can be further reduced to

\[
E_i = 1 + \frac{C_{TOA}}{m C_{aq}} \tag{2.27}
\]

Here \( C_{aq}^* \) is the interfacial concentration of free lactic acid on the aqueous phase side (cf. Figure 2.8b). Note that \( E_i \) in Eq. 2.27 should represent an average value in the microreactor for the estimation of the overall chemical volumetric mass transfer coefficient, \((K_{ov}a)_{Chem}\). Since \( C_{TOA} \) and \( C_{aq}^* \) decreased as reactive extraction progressed along the microreactor, for a first approximation, we can simply take the average concentration between the microreactor inlet and outlet for the evaluation of \( E_i \). That is,

\[
E_i \approx 1 + \frac{\frac{C_{TOA}}{2} + \frac{C_{TOA,1}}{2}}{m \left( \frac{C_{aq}^*,0 + C_{aq}^*,1}{2} \right)} \tag{2.28}
\]
where the subscripts 0 and 1 refer to the microreactor inlet and outlet, respectively. As the interfacial concentrations (i.e., \(C_{aq,0}^*\) and \(C_{aq,1}^*\)) could not be directly measured from the experiments, \(E_i\) is further approximated based on the respective bulk concentrations of lactic acid in the aqueous phase (i.e., \(C_{aq,0}\) and \(C_{aq,1}\)). Therefore,

\[
E_i \approx 1 + \frac{\frac{1}{2} \left( \frac{C_{TOA,0} + C_{TOA,1}}{m} \right)}{\frac{1}{2} \left( \frac{C_{aq,0} + C_{aq,1}}{m} \right)}
\]  

(2.29)

The predicted \(K_{oa, Chem}\) values according to eqs. 2.25 and 2.29 are compared with the experimental measurements for reactive extraction of lactic acid in the microreactors in Figure 2.10. A generally good agreement was observed for both inlet concentrations of lactic acid in the aqueous phase under investigation, indicating that the reactive extraction performance in the current experiments is well described by our developed physical mass transfer model combined with the assumption of an irreversible instantaneous reaction regime. As the bulk concentration of lactic acid in the aqueous phase (i.e., \(C_{aq,0}\) and \(C_{aq,1}\)) was used for the approximation of \(E_i\) in Eq. 2.29 instead of the respective interfacial concentration (i.e., \(C_{aq,0}^*\) and \(C_{aq,1}^*\)), the actual \(E_i\) should be higher and thus the model using Eqs. 2.25 and 2.29 tends to underestimate the

![Figure 2.10](image-url)
experimental measurements if the irreversible instantaneous reaction regime is warranted under the present conditions. However, the overall good agreement revealed in Figure 2.10 suggests that the complexation reaction rate might not be always fast enough to be considered as instantaneous compared with the physical mass transfer rate. In other words, the reaction regime could fall into an instantaneous one near the microreactor inlet and is likely to change into a fast or even slow reaction regime towards the microreactor outlet especially at long residence times at which the equilibrium tends to establish. This indicates a somewhat lower value of the actual enhancement factor than $E_i$ calculated with Eq. 2.28 in the current experiments, as qualitatively considered in Eq. 2.29.

Two local trends seem to exist as can observed in Figure 2.10: (1) at relatively low values of $(K_{ow}\alpha)_{Chem}$ measured in the experiments which correspond to long residence times, the developed model using Eqs. 2.25 and 2.29 seems to overestimate; (2) for 0.055 M lactic acid intake, such overestimation seems more remarkable. Under such circumstances, the equilibrium could be almost approached at significant portions of the microreactor near the outlet. As a result, the reaction rate therein became significantly slow and the average value of the actual enhancement factor could be even lower than the approximation with Eq. 2.29, leading to the observed somewhat significant overestimation in the model predictions.

The overall good agreement between the measured $(K_{ow}\alpha)_{Chem}$ values and model predictions using Eqs. 2.25 and 2.29 further indicates that the simple mass transfer model developed in physical extraction experiments (cf. Eq. 2.18) correctly depicts mass transfer characteristics in the current reactive extraction experiments given similar hydrodynamic conditions in both cases (i.e., slug flow operation, small Fourier numbers and 1:1 aqueous to organic flow ratio). The assumption of an irreversible instantaneous reaction regime, although subject to further validation or improvement due to the lack of detailed kinetic data for complexation reaction between TOA and lactic acid in 1-octanol and the reversible nature of the reaction, satisfactorily captures the interplay between mass transfer and reaction as detailed in Eqs. 2.25 and 2.29. With the developed model, the observed dependence of reactive extraction efficiency on the residence time and inlet concentration of lactic acid can be well explained (Appendix 2C).

### 2.4. Conclusions

Reactive extraction of lactic acid (0.11 M or 0.055 M in water) using 15% (V/V) TOA in 1-octanol was successfully performed under slug flow operation in a capillary microreactors (0.8 mm diameter), which was free from tendency to form emulsions and therefore allows the development
of an alternative method for lactic acid isolation from fermentation broths with fewer operation steps. The extraction of lactic acid approached equilibrium after around 90 s which is considerably faster than our experiments in batch reactors and extraction of other carboxylic acid using TOA in centrifugal contactors. The reactive extraction performance can be satisfactorily described by a simple mass transfer model according to the penetration theory (cf. Eq. 2.18) based on physical extraction experiments conducted in the same microreactor system (acetanilide from water to 1-octanol), combined with an irreversible instantaneous reaction assumption (cf. Eqs. 2.25 and 2.29).

The developed mass transfer model (Eq. 2.18) well describes our physical extraction results in the capillary microreactors under slug flow operation, with just one additional fitting parameter (i.e., 2.6 accounting for the enhancement of internal recirculation in slug flow on mass transfer). In combination with an irreversible instantaneous reaction assumption, the extended mass transfer model (cf. Eqs. 2.25 and 2.29) can describe the experimental measurements in \( K_{ov,a,Chem} \) for reactive extraction of lactic acid with good approximation.

References

(48) Yue, J.; Rebrot, E. V; Schouten, J. C. Enhancement Factor for Gas Absorption in a Finite
Mass transfer characteristics


(53) Partanen, J. I.; Juusola, P. M.; Minkkinen, P. O. Determination of Stoichiometric Dissociation Constants of Lactic Acid in Aqueous Salt Solutions at 291.15 and at 298.15 K. Fluid Phase Equilib. 2003, 204, 245.


Appendices

Appendix 2A. Extraction efficiency as a function of the residence time in physical extraction

With the refined mass transfer model (cf. Eq. 2.18), the fact that the extraction efficiency is only dependent on the residence time in the present physical extraction experiments as shown in Figure 2.2 can be well explained. From Eqs. 2.5 and 2.6, we can derive

\[
C_{aq,0} - C_{aq,1} = \frac{(K_{ov,a})_{phys} V_c}{Q_{aq}} \left[ \frac{C_{aq,1} - C_{org,1}}{m} - \frac{C_{aq,0} - C_{org,0}}{m} \right] Q_{aq} \ln \left( \frac{C_{aq,1} - C_{org,1}}{C_{aq,0} - C_{org,0}} \right)
\]  

(2A.1)

Under the investigated conditions, \(C_{org,0} = 0, \tau = V_c/(Q_{aq} + Q_{org}) = V_c/(2Q_{aq})\). And according to the mass balance, \(C_{org,1} = C_{aq,0} - C_{aq,1}\). Then, it is obtained that

\[
C_{aq,0} - C_{aq,1} = \frac{2\tau (K_{ov,a})_{phys} \left[ C_{aq,1} - \frac{C_{aq,0} - C_{aq,1}}{m} \right] - C_{aq,0}}{\ln \left( \frac{C_{aq,1} - C_{aq,0} - C_{aq,1}}{C_{aq,0}} \right)}
\]  

(2A.2)

The concentration of the solute in the aqueous phase at equilibrium \(C_{aq,eq}\) can be found from

\[
C_{aq,0} - C_{aq,eq} = C_{org,eq} = 0
\]  

(2A.3)

Combining Eq. (2A.3) with Eqs. 2.1 and 2.4, the extraction efficiency for physical extraction can be further written as

\[
\eta = \frac{(m+1)(C_{aq,p} - C_{aq,1})}{mC_{aq,0}} \times 100\%
\]  

(2A.4)

Combining Eqs. (2A.2) and (2A.4) yields
\ln(1-\eta) = -2\tau \left( 1 + \frac{1}{m} \right) (K_m a)_{phys} \quad (2A.5)

By substituting Eq. 2.18 to Eq. (2A.5), it is obtained that

\ln(1-\eta) = -5.2\tau \left( 1 + \frac{1}{m} \right) \left( \frac{1}{2} \frac{D_{aq}}{\pi \tau} \right) \left( \frac{1}{2m} \frac{D_{aq}}{\pi \tau} \right) \left( \frac{4L_{droplet}}{d_{c} (L_{droplet} + L_{slug})} \right) \quad (2A.6)

The above equation clearly corroborates that under the investigated conditions, \( \eta \) is independent of the concentration of acetanilide in the aqueous phase at the microreactor inlet and appears to be only a function of \( \tau \) since the other physical properties of the system are fixed. The shorter the residence time, the lower the extraction efficiency. These analytical results are in good agreement with those shown in Figure 2.2.

**Appendix 2B. Dissociation of lactic acid in the aqueous phase**

According to the dissociation reaction of lactic acid in the aqueous phase (cf. Eq. 2.19), it is satisfied that

\[ K_a = \frac{C_{H^+} C_{L^{\alpha}}}{C_{L^{\alpha}}} \quad (2B.1) \]

\[ C_{L^{\alpha}} + C_{L^{\alpha}} = C_{aq} \quad (2B.2) \]

where \( C_{H^+} \), \( C_{L^{\alpha}} \), \( C_{L^{\alpha}} \) represent the concentrations of \( H^+ \), dissociated lactic acid, free lactic acid at equilibrium in the aqueous phase, respectively. \( C_{aq} \) is the total lactic acid concentration of all forms in the aqueous phase. Under the investigated conditions, \( pH << 7 \). Thus, \( C_{H^+} \approx C_{L^{\alpha}} \) (i.e., the influence of water dissociation is negligible) and it is obtained that

\[ C_{L^{\alpha}} = \frac{-K_a + \sqrt{K_a^2 + 4K_a C_{aq}}}{2} \quad (2B.2) \]
The percentage of the dissociated form of the lactic acid is calculated as \((C_{LA^{-}}/C_{aq}) \times 100\%\). It was found that for 0.11 M lactic acid intake, the percentage of the dissociated form is 3.6% at the microreactor inlet and ranges from 5.5% to 13.4% at the microreactor outlet under the present experimental conditions (the longer the residence time, the higher the percentage of dissociation). For 0.055 M lactic acid intake, the percentage of the dissociated form is 4.9% at the microreactor inlet and ranges from 13.7% to 15.9% at the microreactor outlet. Thus, the average percentage of the dissociated form is below 11% throughout the microreactor. In view of the generally low extent of dissociation under our experimental conditions and to further simplify the model, we neglected the dissociation form of lactic acid in the aqueous phase (i.e., \(C_{LA^{-}} = C_{aq}\)), the refined effect of which on mass transfer will be further considered in our ongoing study.

**Appendix 2C. Extraction efficiency as a function of the residence time and inlet lactic acid concentration in reactive extraction**

The concentration of lactic acid in the aqueous phase when the reactive extraction reaches equilibrium \(C_{aq,eq}\) was obtained from our additional experiments in batch reactors. Lactic acid at a range of concentrations (i.e., 0.1-0.2 M in water) was extracted using 15% (V/V) TOA in 1-octanol as the organic phase. 5 mL of the aqueous phase and 5 mL of the organic phase were stirred in a batch reactor for 18 h at 500 rpm, afterwards the phases were allowed to settle and the aqueous phase was then analyzed to indicate the equilibrium concentration \(C_{aq,eq}\). The following linear relationship was found:

\[
\frac{C_{aq,0} - C_{aq,eq}}{C_{aq,eq}} = 14.27 \quad (2C.1)
\]

Then, the extraction efficiency for reactive extraction under the investigated conditions can be further written as

\[
\eta = \frac{C_{aq,0} - C_{aq,eq}}{C_{aq,0} - C_{aq,eq}} \times 100\% \quad (2C.2)
\]

From Eq. 2.24, we can derive

\[
\ln \frac{C_{aq,0}}{C_{aq,eq}} = \left(\frac{K_{a}}{Q_{aq}}\right)_{Chem} V_c \quad (2C.3)
\]
Under the current conditions, \( \tau = \frac{V_i}{(Q_{aq} + Q_{org})} = \frac{V_i}{2Q_{aq}} \). Combining Eq. (2C.2) and (2C.3) yields

\[
\ln \left( 1 - \left(1 - \frac{1}{15.27} \right) \eta \right) = -2\tau (K_{eq}a)_{Chem} \tag{2C.4}
\]

Substitution of Eq. 25 into Eq. (2C.4) leads to

\[
\ln \left( 1 - \left(1 - \frac{1}{15.27} \right) \eta \right) = -5.2\tau \left( \frac{1}{2} \frac{D_{aq}}{\pi \tau} + \frac{1}{2mE_{org}} \right) \left( \frac{4L_{droplet}}{d_c (L_{droplet} + L_{slug})} \right) \tag{2C.5}
\]

Since it is assumed that the TOA-lactic acid complexes were predominantly in the 1:1 form (cf. Eq. 2.20a), there is according to the mass balance

\[
C_{TOA,0} - C_{TOA,i} = C_{aq,0} - C_{aq,i} \tag{2C.6}
\]

Combining Eq. 2.29 with Eqs. (2C.2) and (2C.6), \( E_i \) can be further approximated as

\[
E_i \approx 1 + \frac{2C_{TOA,0}}{C_{aq,0}} \left( 1 - \frac{1}{15.27} \right) \eta \tag{2C.7}
\]

From Eqs. (2C.5) and (2C.7), it can be seen that under the present reactive extraction experiments (i.e., constant inlet TOA concentration, practically constant interfacial area or droplet(slug lengths, fixed fluid properties), the extraction efficiency (\( \eta \)) only depends on the residence time and the inlet concentration of lactic acid in the aqueous phase (i.e., \( \tau \) and \( C_{aq,0} \)). \( \eta \) increases with increasing \( \tau \). Moreover, the two equations indicate that \( E_i \) and \( \eta \) are both higher at lower \( C_{aq,0} \). The influence of \( C_{aq,0} \) on \( \eta \) should be more obvious at shorter \( \tau \). At sufficiently large \( \tau \), such influence is not discernable since \( \eta \) already approaches 100%. The above findings are in good agreement with the experimental results shown in Figure 2.7.
Appendix 2D. \((K_{ov,a})_{\text{Chem}}\) as a function of the residence time and inlet lactic acid concentration in reactive extraction

Eq. 2.25 predicts that \((K_{ov,a})_{\text{Chem}}\) is a function of \(\tau\) and \(E_i\); \((K_{ov,a})_{\text{Chem}}\) turns to be higher at lower \(\tau\) or at higher \(E_i\). The explanation in Appendix 2C makes it clear that \(E_i\) is higher at lower \(C_{aq,0}\). Therefore, \((K_{ov,a})_{\text{Chem}}\) also depends on \(C_{aq,0}\) and is higher at lower \(C_{aq,0}\). According to Eq. (2C.4), the influence of \(C_{aq,0}\) on \((K_{ov,a})_{\text{Chem}}\) should be more obvious at shorter \(\tau\). In other words, \((K_{ov,a})_{\text{Chem}}\) does not differ much at sufficiently large \(\tau\) for both inlet lactic acid concentrations (i.e., \(C_{aq,0} = 0.11\ M\) and \(0.055\ M\)) since \(\eta\) already approaches 1 in both cases. These discussions well explain the results of the experimentally measured \((K_{ov,a})_{\text{Chem}}\) as depicted in Figure 2.9.

However, according to Eq. 2.25, the predicted \((K_{ov,a})_{\text{Chem}}\) value should increase with increasing \(E_i\) and therefore should increase with decreasing \(C_{aq,0}\) even at sufficient large \(\tau\) values. Such difference in the behavior between the predicted and measured \((K_{ov,a})_{\text{Chem}}\) values is mainly because that the derivation of Eq. 2.25 has neglected the reversible nature of the complexation reaction between lactic acid and TOA. Even with this inadequacy, Eq. 2.25 in combination with Eq. 2.29 can describe the experimental measurements in \((K_{ov,a})_{\text{Chem}}\) with good approximation, which is reasonable since under the majority of our reactive extraction experiments, the reaction in all or at least a large portion of the microreactor is expected to be still far from equilibrium.