Electrochemical membrane-assisted pH-swing extraction and back-extraction of lactic acid

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ARTICLE INFO

ABSTRACT

Reactive extraction of carboxylic acids such as lactic acid with tertiary amines is a state-of-the-art process but suffers strongly from reduced extraction efficiency in buffered environments like fermentation broths. In order to increase the efficiency of *in-situ* product removal, we here propose the combination of a membrane-assisted reactive extraction with an electrochemical pH shift. Prior to extraction in the membrane module, the fermentation broth containing the lactic acid at neutral pH is treated by anodic electrolysis to reduce the pH and thereby improve the extraction yield. Additionally, the cathodic reaction is used to increase the pH of the aqueous stream used for back-extraction of the loaded organic phase.

Model solutions were used to develop a mathematical model, capable of calculating the required membrane area for *in-situ* extractions, considering the effect of the aqueous pH on the extraction performance. Additionally, using electrochemical pH shift, we were able to concentrate lactic acid from 1 wt% in the dilute broth to 7 wt% in the back extract.

1. Introduction

The demand for bio-based chemicals has increased tremendously in the last years [1], and a wide range of pharmaceuticals and chemicals are produced nowadays by fermentation. One example of large-scale fermentatively produced platform chemicals are carboxylic acids, such as lactic acid, mandelic acid, succinic acid, and itaconic acid are surging biobased chemicals [2–5].

Large fermenters are often required since the concentration of the main product in the fermentation broth is low (usually ≪ 10 wt%) due to inhibition of the microorganism by the product and/or the substrate [6]. For pH control during fermentation to counteract acidification due to the produced acids, calcium hydroxide or calcium carbonate is typically used. When the fermentation process is finished, the microorganisms are removed by a filtration step. After that, sulfuric acid is added to release the lactic acid from the lactate form. The free acid is further purified and evaporated into crystalline acid. During this process, calcium sulfate (gypsum) is formed at a rate of about one ton per ton of lactic acid. At

current production levels of lactic acid, still practical uses are found, but especially when acid production is ramped, gypsum production will pose disposal and environmental problems [7,8].

An alternative to the use of neutralizing agents is the *in-situ* separation of the produced acid during fermentation. However, the selective removal of a highly hydrophilic carboxylic acid in the presence of numerous substrates and active microorganisms is challenging. The use of Ionic Liquids (ILs) as solvents is promising due to their negligible vapor pressure, high thermal stability, and low chemical reactivity. Several published ILs proved to have a high capacity and low toxicity towards microorganisms. [9–11]. However, recent work on recovery from ILs showed that direct thermal recovery is not possible at low loadings, and an additional back-extraction is needed, followed by thermal decomposition of the formed complexes [12]. This is less suited for lactic acid, as it is prone to polymerization at elevated temperatures. Therefore, reactive extraction with tertiary amines [3,13–16] still appears to be the solvent of choice. The reactive extraction of carboxylic acid has been subject to numerous studies [7,17,18]. Typically, a
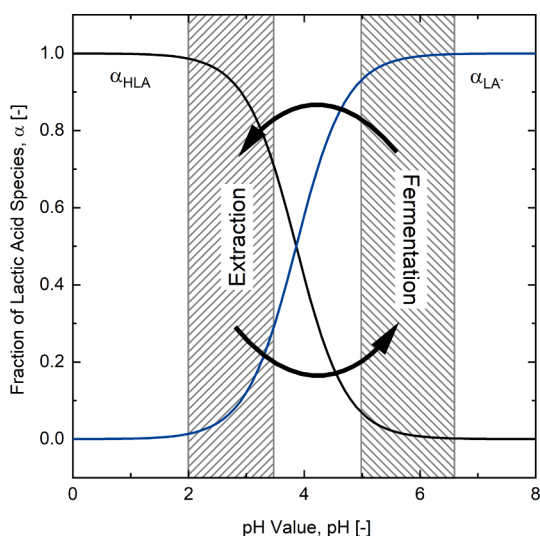

Fig. 1. Optimal ranges of the aqueous pH value for the fermentation and reactive extraction of lactic acid, the blue lines show the reversible pH changes introduced in the cathode/ anode chamber of the electrolysis for optimal fermentation, extraction, and back-extraction. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

tertiary amine like tri-n-octylamine (TOA) is used as an extractant.

However, the pH optima difference for fermentation and extraction poses a significant challenge. While a neutral pH value is required for fermentation, higher extraction yields are achieved at low pH since tertiary amines only extract unprotonated acids. Several publications report the reduced extraction efficiency of tertiary amines at higher pH values [13,14,19,20].

An option to boost the efficiency of tertiary amines at higher pH

values is by adding highly water-soluble salts [21]. However, this approach requires the addition of large amounts of salts and can therefore not be used as an *in-situ* extraction. Thus, this process can only be used for fermentation processes with continuous neutralization or fermentations, which result in low lactic acid concentrations. However, since carboxylic acids are promising platform chemicals used in large-scale, *in-situ* extraction represents the key towards continuous fermentation and, therefore, large-scale production. Another approach to increase the extraction efficiency of tertiary amines is electrochemical pH shift. Recently, separations have been shown in combination with electrochemical stimuli, such as electrodialysis or electro-deionization [4,22,23]. Additionally, recent publications presented combinations of electrochemical separation technologies and bio-based production [24]. For example, electrochemical extraction of carboxylic acid [4,25] or CO_2 capture with amines [26].

Fig. 1 illustrates the correlation of protonation grade and pH for lactic acid.

The positive effect of the combination of electrochemical pH shift and reactive extraction has already been demonstrated by [4]. However, *in-situ* extraction of fermentation broths is challenging due to the formation of stable emulsions, limited phase ratios applicable, and solvent toxicity. A previous publication demonstrated the benefits of a membrane as an extraction interface regarding these issues [3]. We herein combine the concepts of electrochemical pH-swing and membrane-assisted reactive extraction, respectively back-extraction to enable the recovery and up-concentration of lactic acid from aqueous solution at physiological pH values [27]. The relevance of the aqueous pH on the lactic acid extraction performance is investigated experimentally. Based on the experimental observations we derive a mathematical model that takes the weak-acid equilibrium of lactic acid into account and enables design calculations to determine the membrane area required for the extraction at varying pH values in the feed which is an important aspect in the development of well performing *in-situ* separation technologies [28,29].
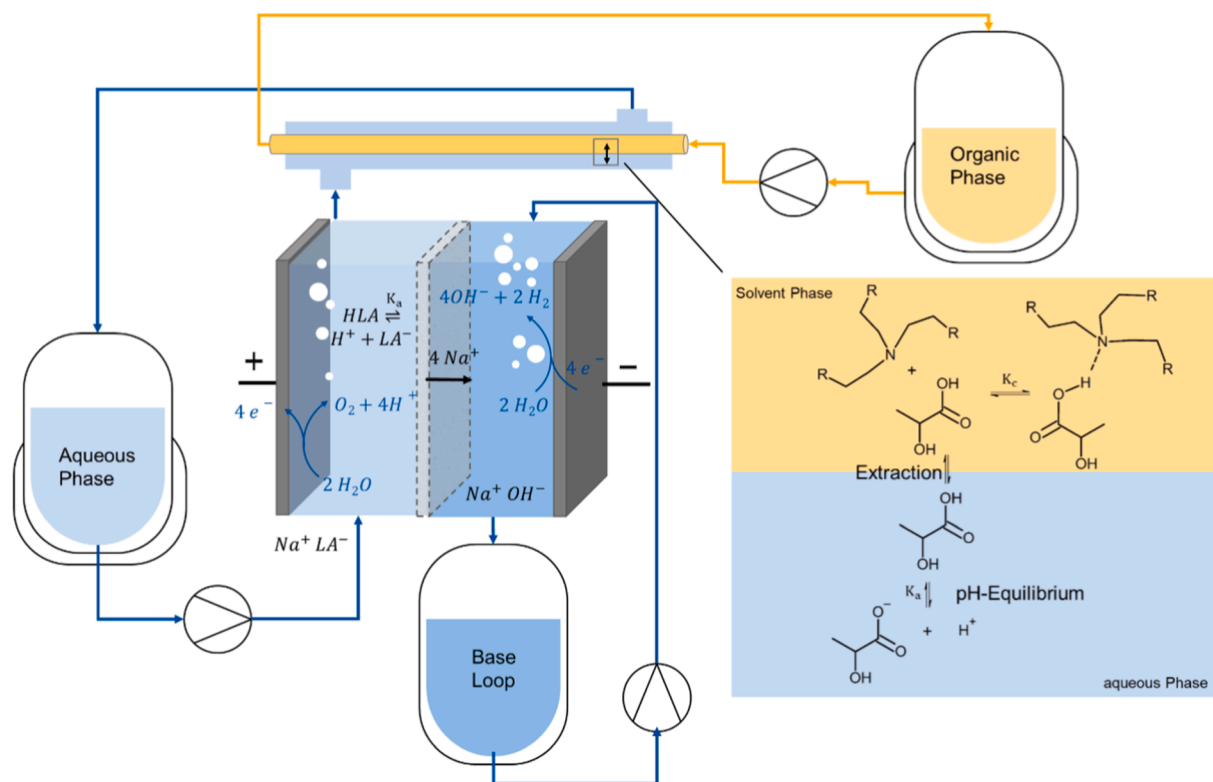

Fig. 2. Electro-swing MSE-Setup and extraction equilibrium system, HLA = protonated lactic acid, K_c = lactic acid-TOA complexation constant, K_a = lactic acid dissociation constant.

Table 1

Used PTFE membrane. The tortuosity was determined using Field Emission Scanning Electron Microscopy (FESEM) as 2.5.

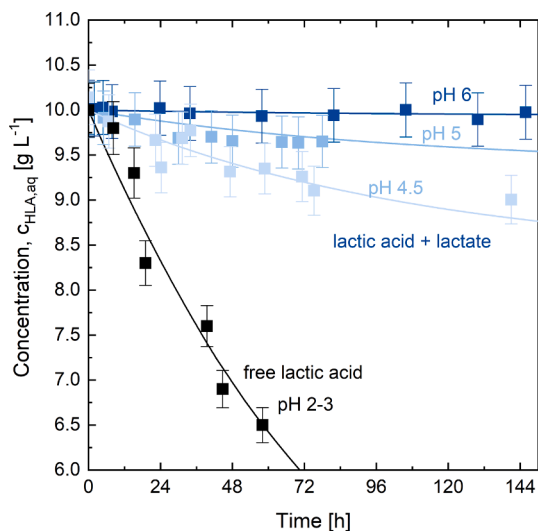| Membrane Material	Porosity [%]	Pore diameter [μm]	Inner Diameter [mm]	Outer diameter [mm]	Wall thickness [μm]
PTFE	54	0.47	2.97	3.49	260

Fig. 3. Aqueous phase lactic acid concentration-in-time-profiles for extractions at initial pH values of pH 6, pH 5, pH 4.5.

2. Materials and methods

2.1. Chemicals

All chemicals used were purchased from Sigma Aldrich Switzerland. Tri-n-octylamine (TOA) (98%), sodium sulfate (>99%), mandelic acid (Standard for quantitative NMR, TraceCERT®), 1-decanol (>99%), sodium hydroxide solution (1 M), sulphuric acid (1 M), deuterium oxide (99.9 atom % D) The aqueous lactic acid solutions were prepared using 85 wt% FCC lactic acid.

2.2. Experimental setup

Fig. 2 shows a schematic representation of the used electro-swing membrane extraction setup. It consists of two temperature-controlled 2 L vessels for the aqueous and organic phases. Two gear pumps (Ismatec Micropump Z − 140, 5 L/h − 60 L/h), were used to pump the phases through the electrochemical cell, the membrane module and back into the container, which can be adjusted to 10–60 °C. Needle valves were used to adjust the pressure. Coriolis flowmeters were used to record the flows as well as the densities of both phases. All phase-contacting parts made from PVDF, PTFE, glass, or stainless steel (1.4404). The electrolysis cathode consists of platinum and the anode of iridium; the electrolysis membrane was a Fumasep FS-990-PK.

A quasi-continuous operation was used to study the pH effect on membrane extraction and potential improvements by applying the electrochemical pH shift. Therefore, the lactic acid containing aqueous phase was first pumped through the anode chamber where the protons produced by the electrolysis acidify the solution before it enters the membrane contactor. The base produced with the electrochemical pH shift was recovered in a 2nd loop (Base loop).

For the back-extraction, the aqueous receiving phase was pumped through the cathode chamber of the electrolysis as depicted in Fig. 7.

2.3. Experimental methods

If not stated differently, 20 wt% tri-n-octylamine (TOA) in 1-decanol was used as solvent for the experiments.

MSE experiments were started by pumping the aqueous phase with an overpressure of about 60 mbar to ambient pressure. Subsequently, the organic phase flow was started, keeping the pressure about 50 mbar lower than the aqueous phase. This avoids the breakthrough of the organic phase into the aqueous phase. Depending on the membrane area used, samples were taken every 1–8 h for analysis.

The organic phase was pumped through the fibers and the aqueous phase through the membrane contactor's shell side. The outer diameter of the fibers was used to calculate the contact area because the hydrophobic membranes are only penetrated by the organic phase.

Table 1 shows the properties of the used PTFE fibers.

Since only a small-sized membrane module (0.059 m^2) was used, both the aqueous and the organic phases were circulated until equilibrium was reached. If not stated otherwise, all experiments were performed at room temperature and with 0.15 M Na$_2$SO$_4$ as background electrolyte, to represent the ionic strength encountered in lactic acid fermentation [30,31].

2.4. Analytic methods

All samples were analyzed by either High-Performance Liquid Chromatography (HPLC) or quantitative Nuclear Magnetic Resonance (NMR) measurements.

Lactic acid concentrations in the preliminary equilibrium study (Fig. A2) were measured by HPLC on an 1100 Series HPLC (Agilent Technologies) equipped with an Organic Acid Resin 250 X 8 mm Column (CS Chromatographie) and a refractive index (RI) detector (G1362A). As mobile phase, 10 mmol H$_2$SO$_4$ at an isochratic flow rate of 1 mL/min was used. Quantitative ^{1}H NMR measurement was used to measure the carboxylic acid concentration in the membrane extraction experiments. Measurements were performed at ambient temperature on a Bruker Avance III 400 NMR spectrometer (Bruker BioSpin AG) fitted with a 5 mm i.d. BBO prodigy probe and operating at 400.13 MHz. Maleic acid was used as an internal standard in D$_2$O.

3. Theory and reactive extraction modeling

Small carboxylic acids are difficult to extract out of aqueous streams due to their hydrophilic nature. Thus, it is highly beneficial to apply a reactive extraction process instead of a conventional physical extraction. Tertiary amines such as tri-n-octylamine (TOA) are state-of-the-art for the reactive extraction of carboxylic acids out of aqueous streams, due to their high selectivity and capacity [13,32–34]. Both are needed when working with fermentation broths since the carboxylic acid is highly diluted (<10 wt% in water) and the fermentation broths contain numerous compounds that preferentially are not co-extracted. The pH of the fermentation broth determines the concentration of protonated lactic acid and thus the extraction rate and efficiency. A mass transfer model was developed to describe the rate of the extraction, and hence, to predict the required membrane area for desired production rates. A detailed description of the model and derivations can be found in the electronic supplementary information (ESI). In Fig. 2, the biphasic reactive extraction model is shown that is used for this work with lactic acid as a model substance [35].

The overall mass transfer coefficient k_{ov} can be determined experimentally from:

$$\dot{n}_{ex} = \frac{dn}{dt} = k_{ov} \cdot A_o \cdot \left([HLA]_{aq} - \frac{[HLA \cdot TOA]_{org}}{K_c \cdot [TOA]_{org}} \right) \quad (1)$$

with K_c as the lactic acid-tri-n-octylamine complexation constant and k_{ov} as the overall mass transfer coefficient and HLAC as the lactic-acid-
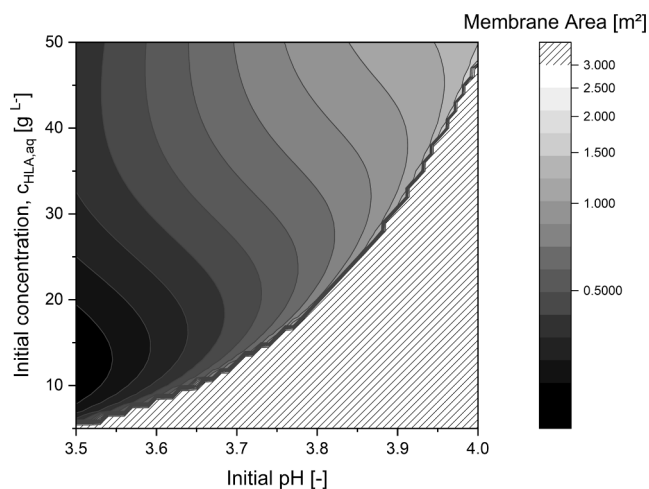
Fig. 4. Membrane area required for the extraction of lactic acid, dependent on pH and total lactic acid concentration.

Fig. 6. Back-extraction with electrochemical pH shift, with LA-saturated 20 wt % tri-n-octylamine in 1-decanol. Electrochemical pH shift to pH 12 prior to back-extraction.

The herein-derived model is based on the classic design approach for membrane-assisted extraction from [39]. For a detailed explanation of the derivation, the reader is referred to the original work and the ESI. In summary, mass balances for a differential volume of the membrane contactor and the overall module are formulated, approximated with a Taylor series expansion and rearranged to yield a differential expression for the membrane area concerning the desired change in lactic acid concentration:

$$\frac{dA_m}{d[HLA]} = - \frac{\frac{\dot{V}_{aq}}{k_{mem}}}{\left([HLA]K_c[TOA] + \frac{\dot{V}_{aq}}{\dot{V}_{org}}\left([HLA_{tot}]_\alpha - [HLA_{tot}] \right) - [HLA_{tot}]_\omega \right)} \quad (2)$$

This approach is analogous to the modeling of plug flow reactors (PFR). Integration of the right-hand side of Equation (2) for the respective concentration $[HLA_{tot}]_\alpha$ at the inlet and at the outlet $[HLA_{tot}]_\omega$, where $[HLA_{tot}]_\omega$ is the desired outlet concentration, yields the required membrane area for the extraction. In order to take into account that only the protonated lactic acid is extracted, the integration variable is altered from the concentration of protonated lactic $[HLA]$ to the total concentration of lactic acid $[HLA_{tot}]$ by changing the integration variable:

$$\frac{dA_m}{d[HLA_{tot}]} = \frac{dA_m}{d[HLA]} \frac{d[HLA]}{d[HLA_{tot}]} \quad (3)$$

The derivation of the differentials resulting from this change of variables is presented in the ESI.

And further:

$$\frac{d[HLA]}{d[HLA_{tot}]} = \frac{[H^+]}{[H^+] + K_a} + [HLA_{tot}]\frac{d[H^+]}{d[HLA_{tot}]}\frac{K_a}{\left([H^+] + K_a\right)^2} \quad (4)$$

The term defined in Equation (4) is in essence the inverse of the aqueous phase enhancement factor as defined by Gössi et al. [36]. A derivation of the remaining differentials caused by the change of the integration variable is given in the ESI (S31, S36). The resulting set of differential expressions equations is solved numerically for the required membrane area using the MATLAB ode15s solver.

4. Results and discussion

Cyclovoltammetry experiments were performed to assess the
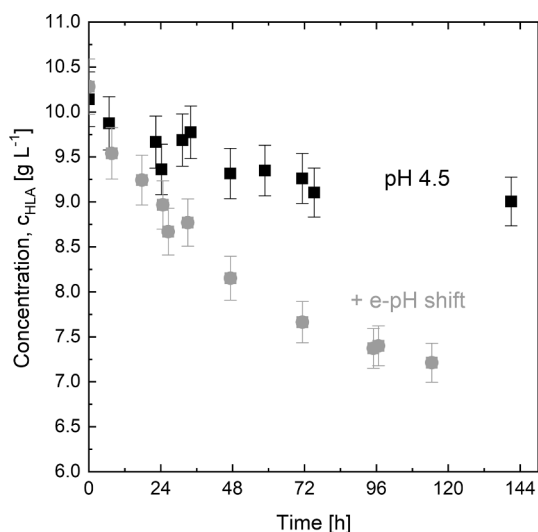

Fig. 5. Aqueous phase lactic acid concentration-in-time-profiles for the extraction with and without electrochemical pH shift.

tri-n-octylamine complex. The bracket is the driving force described by the concentration difference between protonated acid in the aqueous phase $[HLA]_{aq}$ and the organic phase $[HLA]_{org}$. A_o stands for the membrane contact area. It is essential to mention that the membrane only serves as a solid extraction interface, meaning that the membrane does not influence the phase equilibrium in any way. The overall mass transfer coefficient k_{ov} can be calculated as shown in the ESI or can be fitted from mass transfer experiments [36].

The pH of the aqueous is calculated using the dynamic approach [37,38], which includes solving the differential equations for the proton concentration, sulfuric and the lactic acid concentration in the aqueous phase. The constituting equations of the kinetic model used in the calculation presented in Fig. 3 are given in the ESI (S8-S25).

It should be noted that due to the low membrane area and the high volumetric flow, the concentration difference between the membrane inlet and outlet was negligible. Although such settings are well suited to investigate the kinetics of the reactive extraction, a kinetically limited reactive extraction caused by insufficient contact area is not desirable for any process application. For this reason, the calculation of the required membrane area is an essential step in the designing of processes featuring membrane assisted *in-situ* extraction.
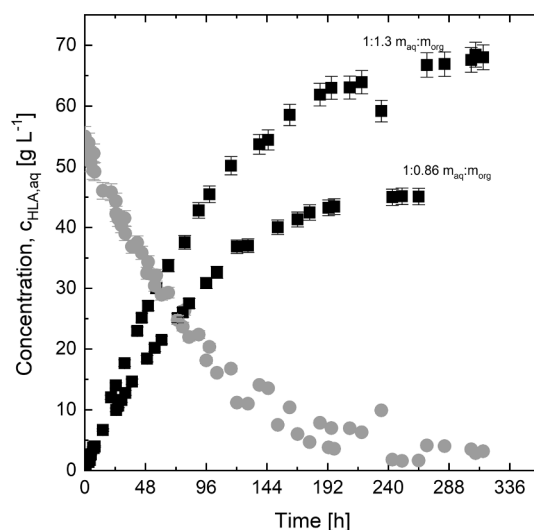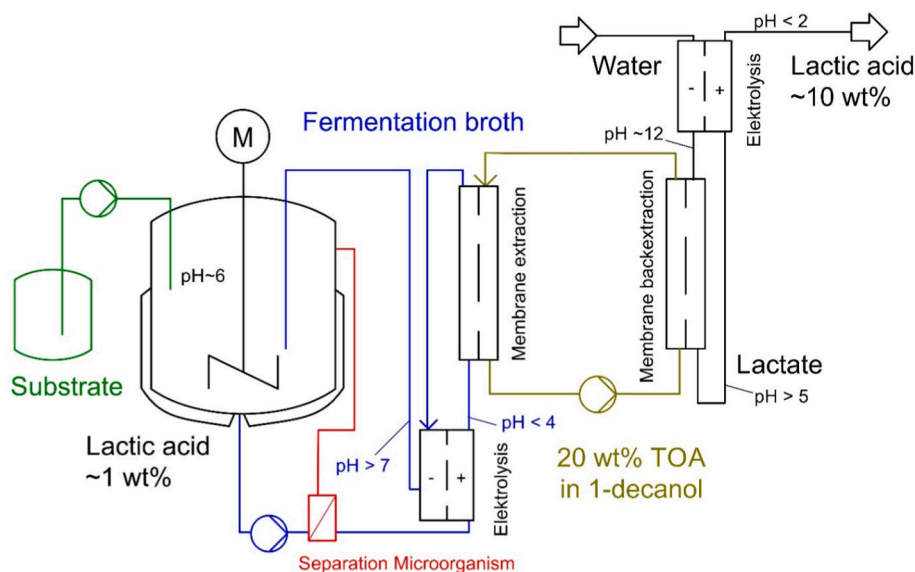
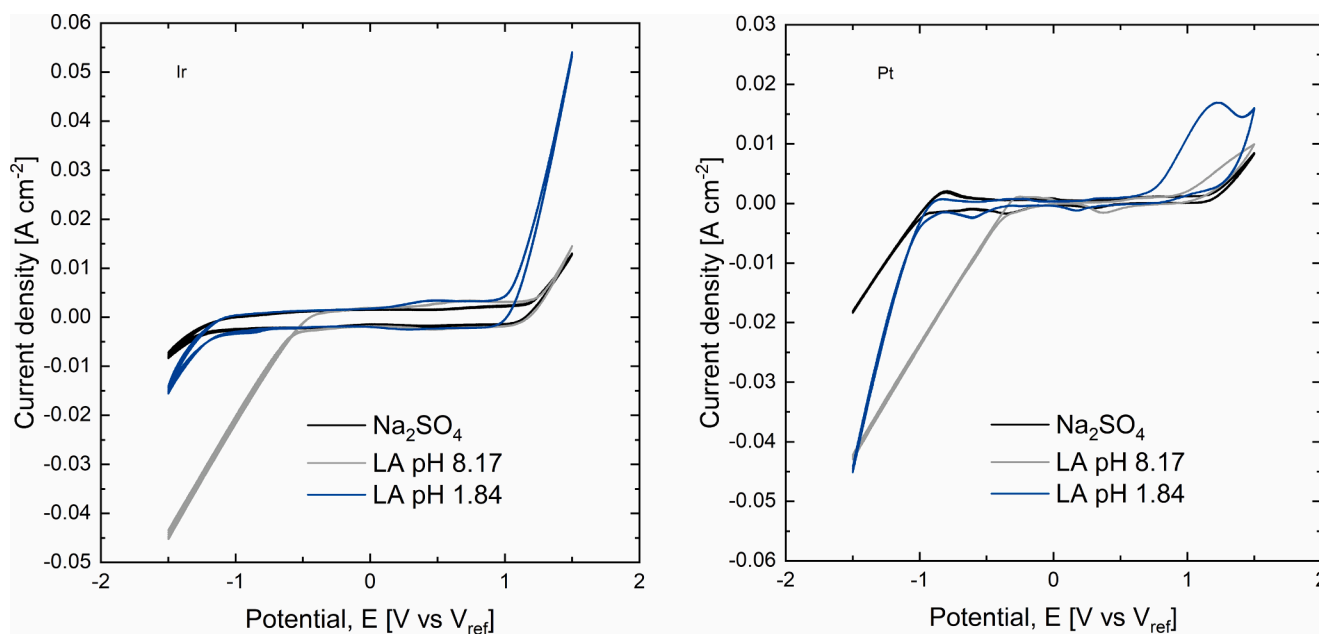**Fig. 7.** Process scheme for the *in-situ* extraction.

Fig. A1. Cyclovoltammetry measurements with a) iridium and b) platinum as anode and cathode material, respectively. 0.083 M sodium sulfate, reference electrode Ag/AgCl. Scan rate 20 mV/s, recorded with a Gamry reference 3000 potentiostat.

stability of lactic acid towards the electrochemical pH-swing. The stability of lactic acid solutions in an operational window of −1.5 to 1.5 V was tested for the alkaline and acid environment. Using platinum as cathode and iridium as anode material, no significant indicators for decomposition were detected. This finding is agrees with the observation that carboxylic acids are often found to be comparatively stable intermediates in the electrochemical degradation of organic compounds [40,41]. However, the electrochemical stability of lactic acid should be validated again at higher current densities and lactic acid concentration, because Chen et al. reported electrochemical degradation of lactic acid at iridium catalysts [42]. More details about the cyclovoltammetry can be found in the Appendix.

4.1. pH-dependent extraction kinetic modeling

The model described in ESI (S8-S25) was experimentally verified. For that, membrane assisted extractions were performed with a membrane contactor with $0.059 \, m^2$ and 1200 g of aqueous phase with 10 g/L lactic acid and 500 g of 20 wt% TOA in 1-Decanol. A lactic acid concentration of 10 g/L represents a realistic concentration during a continuous fermentation with *in-situ* removal.

Both phases were continuously recirculated at 15 kg/h through the membrane until equilibrium was reached. Three experiments were performed at pH 4.5, 5 and 6. A mass transfer coefficient of $2 \cdot 10^{-7}$ m/s working with the same membrane contactor and aqueous feed has been published before [36].

From the results in Fig. 3, it can be concluded that at higher pH values, hardly any extraction is observed.
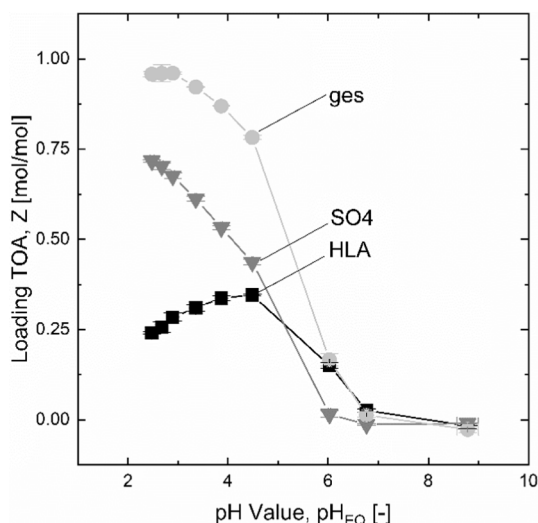
Fig. A2. Loading of tri-n-octylamine (TOA) with lactic acid and sulphuric acid depending on the pH. Lines are only visual help. Initial lactic acid concentration 0.5 mol/L. Initial sodium sulfate concentration 0.15 mol/L. Adjustment of pH using 2 M sulphuric acid.
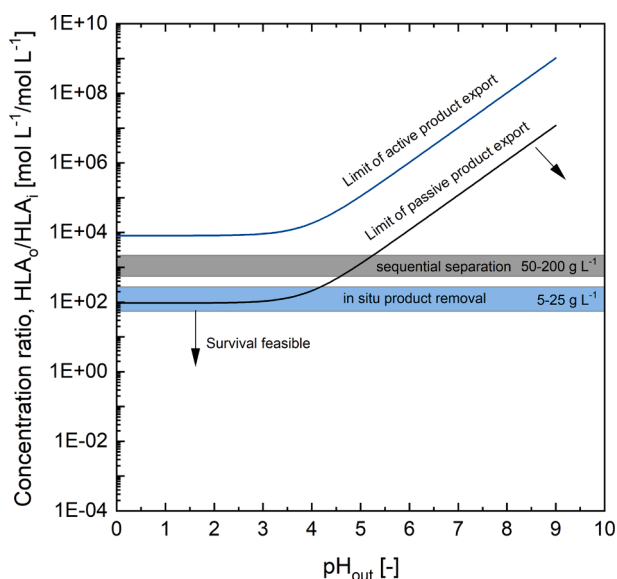

Fig. A3. Curves indicate the thermodynamic limit of the microbial production of lactic acid. Microorganisms relying on passive product export from the cell can only survive at elevated pH and/or lactic acid concentration below 10 g L^{-1}. If the organism is capable of active product export, survival at low pH values is possible at the expense of additional metabolic energy.

While these results are entirely in line with what would be expected based on literature, it proves that using tertiary amines to extract lactic acid from buffered solutions is highly inefficient [20,43].

Fig. 3 shows the experimental and simulative results for various pH values, the initial lactic acid concentration was 10 g/L, and the organic phase consisted of 20 wt% TOA in 1-decanol. The black line represents the predicted concentration profile using the model from [39] without any pH-dependency included. The blue lines show the predicted concentration profiles based on the model presented in this work, which can be regarded as a further development of the models from [4,36]. The experimental and simulative results are in excellent agreement. It is evident that the aqueous pH has a striking effect on the kinetics of the membrane-assisted extraction. Therefore, it is crucial to consider its

impact in the design process and maintain a suitable pH during the operation to ensure satisfying extraction rates. This can either be done by employing the electrochemical pH shift prior to extraction or by developing acid tolerant strains of lactic acid producing microorganisms [44–46].

4.2. Design of membrane contactor area with regard to pH

The classical design equations which are used to calculate the membrane area required for the membrane supported extraction do not consider the pH effect imposed on the extraction by the weak-acid equilibrium [39]. Based on the modeling results we extended the design framework developed by Melin et al. and derived a new mathematical model to calculate the membrane area required for ISPR at different feed conditions (concentration and pH). Fig. 4 shows the required areas for a fictive fermenter of 10 L operated with a productivity of 2 g/Lh, depending on the pH and lactic acid concentration. In the hatched area, the pH equilibrium prohibits the complete extraction and causes a steep exponential increase of the required membrane area, which makes the junction region sensitive towards numerical errors.

Two major influences can be identified in Fig. 4: The reduced membrane area required at low acid concentrations and the strong influence of the pH value. The first influence can be explained by the higher amine-acid ratio at low concentrations, which is also reflected in the last term of Equation S13 in the ESI. The increasing enhancement factor outweighs the decreasing driving force at low concentrations and leads to higher mass transfer rates. This also demonstrates that the reactive extraction with tertiary amines is especially suitable for *in-situ* extractions, where lactic acid must be recovered from low concentrations [47,48].

The second influence, the influence of the pH on the required membrane contact area, is apparent, demonstrating the immense improvement that could be reached when applying an electrochemical pH shift or. The membrane area required for extraction rises exponentially when the aqueous pH approaches 4. Above this pH, the removal of protonated lactic acid causes an immediate increase of the aqueous pH, which triggers the dissociation of the remaining lactic acid and thereby makes it unavailable for extraction. A starting pH well below 4 is mandatory to achieve an efficient extraction. This requirement is not compatible with the thermodynamic limits imposed by microbial lactic acid production and product export from the cell in currently used microorganisms (Fig. A3) [49]. As a consequence, there is a gap between the optimal operational conditions required for fermentation and extraction with regard to the pH value, which can be closed by electrochemical pH shift. By doing so, the pH of the aqueous solution can be reduced prior to the membrane module and the extraction efficiency can be highly increased. Fig. 5 shows the influence of an electrochemical pH shift from pH 4.5 to pH 4. In both experiments, the initial lactic acid concentration was 10 g/L, and the organic phase consisted of 20 wt% TOA in 1-decanol. The black symbols represent an experiment with an initial pH of 4 and without electrochemical pH-swing, the grey symbols an experiment in which the pH of the aqueous feed phase was reduced in the electrochemical cell prior to the membrane-assisted extraction to a pH 4.

The improvement depicted in Fig. 5 is apparent. However, the benefit can be even: The electrolysis allows a change of pH at a given lactic acid concentration and can therefore lead to strongly reduced membrane contactor sizes required.

The electrochemical pH shift improves the extraction rate at the expense of electric power consumption. The degree of the pH shift depends on the amount of protons $\dot{n}_{H^+}$ produced in the electrolysis and is proportional to the electric current I according to Faraday's law:

$$\dot{n}_{H^+} = \frac{I \cdot t}{z \cdot F}$$

With t being the time, z the number of electrons transferred in the

electrochemical reaction and F being the Faraday constant. As a consequence, a high degree of pH shift requires a high input of electricity. This results in a trade-off between the power consumption required for the pH shift and the membrane area required for extraction. Finding the sweet spot for the process operation thus requires an understanding of the relation between the membrane area required for extraction and its dependence on the initial lactic acid concentration and the initial pH at the module entrance. For this purpose, we used the design method presented in Section 3 and the ESI to calculate the required membrane area with regard to the initial condition at the module entrance.

Fig. 5 implies that a lower pH value is always better for extraction. However, culture media typically contain various salts, like NaCl, Na$_2$SO$_4$, or K$_2$HPO$_4$. Their presence should initiate the salting-out of the produced acids and increase the distribution coefficient. Contrarily, studies showed that the presence of salts reduces the extraction efficiency of carboxylic acids [43,50]. For example, sodium chloride results in the formation of hydrochloric acid, which then competes with lactic acid for extraction. This leads to a reduced extraction efficiency. Therefore, the number of undissociated acids in the fermentation broth should be kept at a minimum to reduce co-extraction. Further information about the co-extraction of salts can be found in the Appendix, Fig. A2. As an alternative, the extractant Trioctylphosphine oxide (TOPO) showed only negligible co-extraction of sulphuric acid and thus might be a promising alternative to TOA [51].

Another opportunity to close the gap between the fermentation and extraction pH values is the development of more acid-resistant bacteria, which have been investigated lately [45]. These microorganisms allow a more efficient extraction process due to an increased driving force and reduced electrolysis's required power input. If low pH tolerant strains are available [14,45], the direct extraction of lactic acid is viable without an electrochemical pH shift prior to extraction. However, at low pH, the lactic acid production and export from the cell of the biocatalyst require additional metabolic energy for the active product export. This energy is inevitably gained at the expense of substrate yield, which causes a trade-off between ease of separation and substrate utilization efficiency [49]. Nevertheless, using an electrochemical pH shift in the back-extraction process will still be highly beneficial. The following section describes this back-extraction approach in detail.

4.3. Electrochemical pH-swing back-extraction

A continuous process raises the need for a continuous solvent recycling process; thus, a back-extraction is needed. Different strategies have been reported for the back-extraction of carboxylic acids out of tertiary amines. In the case of volatile acids or solvents, the most straightforward option appears to be evaporation or distillation. A temperature- and solvent-swing process can be applied if neither the carboxylic acid or the solvent is volatile [18]. Since the complexes are stabilized by hydrogen bonds with the solvent n-decanol, adding a solvent that cannot donate or accept hydrogen bonds - like heptane - reduces the complex's stability [18,52,53]. Additionally, an increase in the organic phase temperature reduces the complexation constant, increasing the recovery rate [52,54]. However, the added heptane needs to be recycled after back-extraction by evaporation [3]. Therefore, we propose using an electrochemical pH shift for the back-extraction. Back-extraction with a receiving phase at alkaline pH conditions is known for its high efficiency [28]. In our setup the alkaline conditions in the receiving phase are established by pumping the receiving phase through the cathode chamber of an electrolysis cell. Experiments with lactic-acid saturated 20 wt% TOA in 1-decanol (55 g/L lactic acid) and an aqueous receiving phase with 0.15 M Na$_2$SO$_4$ set to a pH of 12 led to extraction efficiencies of > 90%. Fig. 6 shows the back-extraction process using an electrochemical pH shift to increase the pH of the receiving aqueous phase to 12 before the actual back-extraction.

Compared to the temperature- and solvent-swing process, the mass transfer coefficient is reduced when applying an electrochemical pH shift: The mass transfer coefficient with temperature- and solvent-swing is 2.1*10^{-7} m/s (Solvent/Feed/Wash with a volumetric ratio of 1/1/3), and 1.4*10^{-7} m/s with the electrochemical pH shift (Solvent/Feed with a 1/1 volumetric ratio). The reduced viscosity with heptane as antisolvent and working at increased temperature can explain the increased extraction rate. However, the extraction efficiency with pH shift can be increased significantly, from ∼ 40% [3] to > 90%, depending on the chosen parameters. Thus, by applying an electrochemical pH shift, a much higher concentration factor is achievable. Moreover, the subsequent distillation process for water removal requires less energy, and the whole process becomes more energy efficient. Additionally, evaporating three parts of antisolvent per part extractant phase after back-extraction is no longer necessary.

4.4. Outlook

Based on the results presented in this work we propose combination of membrane supported extraction and electrochemical pH-swing for both the extraction and backextraction process.

Fig. 7 shows the process flow diagram for a continuous fermentation process with *in-situ* removal of lactic acid. By pumping the fermentation broth through the anode chamber, the pH can be reduced before the extraction.

Further investigation is required with actual fermentation broths and its influence on the electrolysis. *In-situ* extraction with membrane supported extraction have been previously reported by [3].

5. Conclusion

The developed pH-dependent reactive extraction model enables the calculation of the necessary contact area for membrane-assisted extraction, an essential step in the design of extraction processes to separate lactic and other carboxylic with membrane contactors. Implementing a pH shift electrolysis can overcome the pH gap between the optimal operating conditions of fermentation and extraction, reducing the required membrane. The significant reduction of the required area is advantageous since membrane contactors often represent substantial investment costs. The presented electrochemically driven back-extraction enables high concentration factors reducing the required energy input for thermal purification tremendously.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix

Cyclic voltammetry measurements are shown in Fig. A1:

Fig. A1 a) shows that the lactic acid profile in the negative voltage range drops earlier than the reference measurement with sodium sulfate. However, in the voltage range of interest (1–1.5 V), the two profiles coincide. We can therefore conclude that with iridium as anode material, the chemical stability of the lactic acid during electrolysis can be ensured.

Fig. A1 b) shows a number of small peaks in the range from −1 to 1 V. The same peaks can be found in the reference measurement, indicating material-typical reactions of the electrode. However, the peak in the lactic acid profile at 1.2 V does not agree with the reference measurement, which indicates an electrochemical degradation of the lactic acid at the platinum anode. On the other side, no reaction peak is observed for an alkaline pH at the negative potential for platinum. Thus, platinum is considered a suitable cathode material.

An optimal pH range for lactic acid extraction needs to be found. For this purpose, a titration experiment was performed. A 0.5 M lactic acid solution with a sodium sulfate concentration of 0.15 mol/L was used as raffinate phase. Using sodium hydroxide, the pH was set to a basic value. During the experiment, the pH value was gradually lowered by the addition of a titration solution. The loading of TOA as a function of pH is shown in Fig. A2. The figure includes the loading with lactic acid (Z_{HLA}) and sulfate (Z_{SO4}). Up to a pH of 6, mainly lactic acid is extracted. However, the obtained yield is low since most of the acid is deprotonated and doesn't take part in extraction.

The yield can be increased by lowering pH. At the same time, the loading of TOA with sulfate rises as well. The highest yield for lactic acid is reached at a pH of 4.5. A Z_{HLA} value of 0.35 is achieved. This corresponds to 70% of the maximum value. Lowering the pH further causes the yield to decrease. When reaching a pH of 2.5 Z_{HLA} is 0.24. Therefore, the optimal pH for extraction of lactic with pH adjustment using sulphuric acid is 4.5. When choosing a higher pH range, the driving force for extraction decreases significantly due to dissociation. For low pH ranges, the influence of co-extraction increases.

Fig. A3 presents the thermodynamic limits of microbial lactic acid production and product export from the cell. The calculation for the limits is based on considerations of [49] and [55]. An intracellular pH of about 7 and an intracellular lactic acid concentration in the order of 0.001 mol/L is assumed. Furthermore, a proton motive over the cell membrane of 150 mV and an energy gain per mole ATP hydrolyzed of 40 kJ/mol is selected, as suggested [49].

$$\frac{HLA_{tot,o}}{HLA_{tot,i}} = 10^{\left(\frac{F(n-1)(-pmf)}{RT\ln(10)} + pH_o - pH_i + m \cdot \frac{\Delta G_{ATP}}{RT\ln(10)}\right)} \cdot \frac{1 + 10^{(pKs - pH_o)}}{1 + 10^{(pKs - pH_i)}} \tag{E1}$$

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.seppur.2022.120702.

References

[1] A. Kuznetsov, A. Beloded, A. Derunets, V. Grosheva, L. Vakar, R. Kozlovskiy, V. Shvets, Biosynthesis of lactic acid in a membrane bioreactor for cleaner technology of polylactide production, Clean Technol. Environ Policy. 19 (3) (2017) 869–882, https://doi.org/10.1007/s10098-016-1275-z.

[2] J. Vijayakumar, R. Aravindan, T. Viruthagiri, Recent trends in the production, purification and application of lactic acid, Chem. Biochem. Eng. Q. 22 (2008) 245–264.

[3] A. Gössi, F. Burgener, D. Kohler, A. Urso, B.A. Kolvenbach, W. Riedl, B. Schuur, In-situ recovery of carboxylic acids from fermentation broths through membrane supported reactive extraction using membrane modules with improved stability, Sep. Purif. Technol. 241 (2020) 116694, https://doi.org/10.1016/j.seppur.2020.116694.

[4] M. Gausmann, C. Kocks, M. Doeker, A. Eggert, T. Maßmann, A. Jupke, Recovery of succinic acid by integrated multi-phase electrochemical pH-shift extraction and crystallization, Sep. Purif. Technol. 240 (2020) 116489, https://doi.org/10.1016/j.seppur.2019.116489.

[5] N. Murali, K. Srinivas, B.K. Ahring, Biochemical production and separation of carboxylic acids for biorefinery applications, MDPI AG 3 (2) (2017) 22, https://doi.org/10.3390/fermentation3020022.

[6] M. Othman, A.B. Ariff, L. Rios-Solis, M. Halim, Extractive fermentation of lactic acid in lactic acid bacteria cultivation: A review, Front. Microbiol. 8 (2017) 2285, https://doi.org/10.3389/fmicb.2017.02285.

[7] D. Yankov, J. Molinier, J. Albet, G. Malmary, G. Kyuchoukov, Lactic acid extraction from aqueous solutions with tri-n-octylamine dissolved in decanol and dodecane, Biochem. Eng. J. 21 (1) (2004) 63–71, https://doi.org/10.1016/j.bej.2004.03.006.

[8] H.G. Joglekar, I. Rahman, S. Babu, B.D. Kulkarni, A. Joshi, Comparative assessment of downstream processing options for lactic acid, Sep. Purif. Technol. 52 (1) (2006) 1–17, https://doi.org/10.1016/j.seppur.2006.03.015.

[9] F.S. Oliveira, J.M.M. Araújo, R. Ferreira, L.P.N. Rebelo, I.M. Marrucho, Extraction of l-lactic, l-malic and succinic acids using phosphonium-based ionic liquids, Sep. Purif. Technol. 85 (2012) 137–146, https://doi.org/10.1016/j.seppur.2011.10.002.

[10] K. Tonova, I. Svinyarov, M.G. Bogdanov, Hydrophobic 3-alkyl-1-methylimidazo-lium saccharinates as extractants for l-lactic acid recovery, Sep. Purif. Technol. 125 (2014) 239–246, https://doi.org/10.1016/j.seppur.2014.02.001.

[11] J. Martak, S. Schlosser, Extraction of lactic acid by phosphonium ionic liquids, Sep. Purif. Technol. 57 (3) (2007) 483–494, https://doi.org/10.1016/j.seppur.2006.09.013.

[12] E. Reyhanitash, E. Fufachev, K.D. van Munster, M.B.M. van Beek, L.M.J. Sprakel, C. N. Edelijn, B.M. Weckhuysen, S.R.A. Kersten, P.C.A. Bruijnincx, B. Schuur, Recovery and conversion of acetic acid from a phosphonium phosphinate ionic liquid to enable valorization of fermented wastewater, Green Chem. 21 (8) (2019) 2023–2034.

[13] B. Choudhury, T. Swaminathan, Lactic acid extraction with trioctyl amine, Bioprocess Eng. 19 (1998) 317–320, https://doi.org/10.1007/s004490050526.

[14] D. Yankov, J. Molinier, G. Kyuchoukov, J. Albet, G. Malmary, Improvement of the lactic acid extraction. Extraction from aqueous solutions and simulated fermentation broth by means of mixed extractant and TOA, partially loaded with HCl, Chem. Biochem. Eng. Q. 19 (2005) 17–24. https://www.researchgate.net/publication/237386284_Improvement_of_the_Lactic_Acid_Extraction_Extraction_From_Aqueous_Solutions_and_Simulated_Fermentation_Broth_by_Means_of_Mixed_Extractant_and_TOA_Partially_Loaded_with_HCl (accessed June 26, 2020).

[15] A. Krzyzaniak, B. Schuur, M. Sukumaran, H. Zuilhof, A.B. De Haan, Extractant screening for liquid-liquid extraction in environmentally benign production routes, Chem. Eng. Trans. 24 (2011) 709–714, https://doi.org/10.3303/CET1124119.

[16] V. Inyang, D. Lokhat, Reactive Extraction of Malic Acid using Trioctylamine in 1–Decanol: Equilibrium Studies by Response Surface Methodology Using Box Behnken Optimization Technique, Sci. Rep. 10 (1) (2020), https://doi.org/10.1038/s41598-020-59273-z.

[17] Z. Zhou, Z. Li, W. Qin, Reactive extraction of saturated aliphatic dicarboxylic acids with trioctylamine in 1-octanol: Equilibria, model, and correlation of apparent reactive equilibrium constants, Ind. Eng. Chem. Res. 52 (31) (2013) 10795–10801, https://doi.org/10.1021/ie4008002.

[18] L.M.J. Sprakel, B. Schuur, Solvent developments for liquid-liquid extraction of carboxylic acids in perspective, Sep. Purif. Technol. 211 (2019) 935–957, https://doi.org/10.1016/j.seppur.2018.10.023.

[19] J.A. Tamada, A.S. Kertes, C.J. King, Extraction of Carboxylic Acids with Amine Extractants. 1. Equilibria and Law of Mass Action Modeling, Ind. Eng. Chem. Res. 29 (7) (1990) 1319–1326, https://doi.org/10.1021/ie00103a035.

[20] S.T. Yang, S.A. White, S.T. Hsu, Extraction of Carboxylic Acids with Tertiary and Quaternary Amines: Effect of pH, Ind. Eng. Chem. Res. 30 (6) (1991) 1335–1342, https://doi.org/10.1021/ie00054a040.

[21] P. Baral, A. Pundir, A. Kurmi, R. Singh, V. Kumar, D. Agrawal, Salting-out assisted solvent extraction of L (+) lactic acid obtained after fermentation of sugarcane

bagasse hydrolysate, Sep. Purif. Technol. 269 (2021) 118788, https://doi.org/10.1016/j.seppur.2021.118788.

[22] L. Handojo, A.K. Wardani, D. Regina, C. Bella, M.T.A.P. Kresnowati, I.G. Wenten, Electro-membrane processes for organic acid recovery, RSC Adv. 9 (14) (2019) 7854–7869, https://doi.org/10.1039/C8RA09227C.

[23] C. Kocks, J. Görtz, M. Gausmann, A. Jupke, Electrochemically induced downstream processes for dicarboxylic acids reduce neutral salt emission, Chemie Ing. Tech. 92 (9) (2020) 1175–1176, https://doi.org/10.1002/cite.202055050.

[24] F. Harnisch, C. Urban, Electrobiorefineries: Unlocking the Synergy of Electrochemical and Microbial Conversions, Angew. Chemie - Int. Ed. 57 (32) (2018) 10016–10023, https://doi.org/10.1002/anie.201711727.

[25] W.C. Khor, S. Andersen, H. Vervaeren, K. Rabaey, Electricity-assisted production of caproic acid from grass, Biotechnol. Biofuels. 10 (2017) 180, https://doi.org/10.1186/s13068-017-0863-4.

[26] J.S. Kang, S. Kim, T.A. Hatton, Redox-responsive sorbents and mediators for electrochemically based CO2 capture, Curr. Opin. Green Sustain. Chem. 31 (2021) 100504.

[27] S.A.A. Rawoof, P.S. Kumar, D.-V. Vo, K. Devaraj, Y. Mani, T. Devaraj, S. Subramanian, Production of optically pure lactic acid by microbial fermentation: a review, Environ. Chem. Lett. 19 (1) (2021) 539–556, https://doi.org/10.1007/s10311-020-01083-w.

[28] K. Meng, G. Zhang, C. Ding, T. Zhang, H. Yan, D. Zhang, T. Fang, M. Liu, Z. You, C. Yang, J. Shen, X. Jin, Recent Advances on Purification of Lactic Acid, Chem. Rec. 20 (11) (2020) 1236–1256, https://doi.org/10.1002/tcr.202000055.

[29] W. Van Hecke, G. Kaur, H. De Wever, Advances in in-situ product recovery (ISPR) in whole cell biotechnology during the last decade, Biotechnol. Adv. 32 (7) (2014) 1245–1255, https://doi.org/10.1016/j.biotechadv.2014.07.003.

[30] L.M.D. Gonçalves, M.T.O. Barreto, A.M.B.R. Xavier, M.J.T. Carrondo, J. Klein, Inert supports for lactic acid fermentation -a technological assessment, Appl. Microbiol. Biotechnol. 38 (1992) 305–311, https://doi.org/10.1007/BF00170077.

[31] M.G. Gänzle, M. Ehmann, W.P. Hammes, Modeling of growth of Lactobacillus sanfranciscensis and Candida milleri in response to process parameters of sourdough fermentation, Appl. Environ. Microbiol. 64 (7) (1998) 2616–2623.

[32] A. Krzyzaniak, M. Leeman, F. Vossebeld, T.J. Visser, B. Schuur, A.B. De Haan, Novel extractants for the recovery of fermentation derived lactic acid, Sep. Purif. Technol. 111 (2013) 82–89, https://doi.org/10.1016/j.seppur.2013.03.031.

[33] C.S. López-Garzón, A.J.J. Straathof, Recovery of carboxylic acids produced by fermentation, Biotechnol. Adv. 32 (5) (2014) 873–904, https://doi.org/10.1016/j.biotechadv.2014.04.002.

[34] I.S. Udachan, A.K. Sahoo, A study of parameters affecting the solvent extraction of lactic acid from fermentation broth, Brazilian J Chem. Eng. 31 (3) (2014) 821–827, https://doi.org/10.1590/0104-6632.20140313s00002495.

[35] B. Schuur, J.G.M. Winkelman, H.J. Heeres, Equilibrium studies on enantioselective liquid - liquid amino acid extraction using a cinchona alkaloid extractant, Ind. Eng. Chem. Res. 47 (24) (2008) 10027–10033, https://doi.org/10.1021/ie800668e.

[36] A. Gössi, W. Riedl, B. Schuur, Mass transfer analysis and kinetic modeling for process design of countercurrent membrane supported reactive extraction of carboxylic acids, Chem. Eng. Sci. X. 13 (2022) 100119, https://doi.org/10.1016/j.cesx.2021.100119.

[37] J. Schell, E. Zars, C. Chicone, R. Glaser, Simultaneous Determination of All Species Concentrations in Multiequilibria for Aqueous Solutions of Dihydrogen Phosphate Considering Debye-Hückel Theory, J. Chem. Eng. Data. 63 (6) (2018) 2151–2161, https://doi.org/10.1021/acs.jced.8b00146.

[38] E. Zars, J. Schell, M.A. Delarosa, C. Chicone, R. Glaser, Dynamical Approach to Multi-Equilibria Problems Considering the Debye-Hückel Theory of Electrolyte Solutions: Concentration Quotients as a Function of Ionic Strength, J. Solution Chem. 46 (3) (2017) 643–662, https://doi.org/10.1007/s10953-017-0593-z.

[39] T. Melin, R. Rautenbach, Membranverfahren, Springer Berlin Heidelberg, 2007. https://doi.org/10.1007/978-3-540-34328-8.

[40] L. Ostervold, S.I. Perez Bakovic, J. Hestekin, L.F. Greenlee, Electrochemical biomass upgrading: Degradation of glucose to lactic acid on a copper(ii) electrode, RSC Adv. 11 (2021) 31208–31218, https://doi.org/10.1039/d1ra06737k.

[41] D. DiMarino, T. Jestel, C. Marks, J. Viell, M. Blindert, S.M.A. Kriescher, A.C. Spiess, M. Wessling, Carboxylic Acids Production via Electrochemical Depolymerization of Lignin, ChemElectroChem. 6 (5) (2019) 1434–1442, https://doi.org/10.1002/celc.201801676.

[42] C. Chen, A.J. Bloomfield, S.W. Sheehan, Selective Electrochemical Oxidation of Lactic Acid Using Iridium-Based Catalysts, Ind. Eng. Chem. Res. 56 (13) (2017) 3560–3567, https://doi.org/10.1021/acs.iecr.6b05073.

[43] K.L. Wasewar, Reactive Extraction: An Intensifying Approach for Carboxylic Acid Separation, Int. J. Chem. Eng. Appl. 3 (2012) 249–255, https://doi.org/10.7763/ijcea.2012.v3.195.

[44] M. Singhvi, T. Zendo, K. Sonomoto, Free lactic acid production under acidic conditions by lactic acid bacteria strains: challenges and future prospects, Appl. Microbiol. Biotechnol. 102 (14) (2018) 5911–5924, https://doi.org/10.1007/s00253-018-9092-4.

[45] H.J. Park, J.H. Bae, H.J. Ko, S.H. Lee, B.H. Sung, J.I. Han, J.H. Sohn, Low-pH production of d-lactic acid using newly isolated acid tolerant yeast Pichia kudriavzevii NG7, Biotechnol. Bioeng. 115 (2018) 2232–2242, https://doi.org/10.1002/bit.26745.

[46] A.N. Marchesan, J.F. Leal Silva, R. Maciel Filho, M.R. Wolf Maciel, Techno-Economic Analysis of Alternative Designs for Low-pH Lactic Acid Production, ACS Sustain Chem. Eng. 9 (36) (2021) 12120–12131, https://doi.org/10.1021/acssuschemeng.1c03447.

[47] N. Tik, E. Bayraktar, U. Mehmetoglu, In situ reactive extraction of lactic acid from fermentation media, J. Chem. Technol. Biotechnol. 76 (7) (2001) 764–768, https://doi.org/10.1002/jctb.449.

[48] M. Boonmee, O. Cotano, S. Amnuaypanich, N. Grisadanurak, Improved Lactic Acid Production by In Situ Removal of Lactic Acid During Fermentation and a Proposed Scheme for Its Recovery, Arab. J. Sci. Eng. 41 (6) (2016) 2067–2075, https://doi.org/10.1007/s13369-015-1824-5.

[49] A.J.A.V. Maris, W.N. Konings, J.P.V. Dijken, J.T. Pronk, Microbial export of lactic and 3-hydroxypropanoic acid: Implications for industrial fermentation processes, Metab. Eng. 6 (4) (2004) 245–255, https://doi.org/10.1016/j.ymben.2004.05.001.

[50] B.S. Kim, Y.K. Hong, W.H. Hong, Effect of salts on the extraction characteristics of succinic acid by predispersed solvent extraction, Biotechnol Bioprocess Eng. 9 (3) (2004) 207–211, https://doi.org/10.1007/BF02942294.

[51] T. Brouwer, M. Blahusiak, K. Babic, B. Schuur, Reactive extraction and recovery of levulinic acid, formic acid and furfural from aqueous solutions containing sulphuric acid, Sep. Purif. Technol. 185 (2017) 186–195, https://doi.org/10.1016/j.seppur.2017.05.036.

[52] Y.K. Hong, W.H. Hong, D.H. Han, Application of reactive extraction to recovery of carboxylic acids, Biotechnol Bioprocess Eng. 6 (6) (2001) 386–394, https://doi.org/10.1007/BF02932319.

[53] L.M.J. Sprakel, B. Schuur, Improving understanding of solvent effects on intermolecular interactions in reactive liquid–liquid extraction with Isothermal Titration Calorimetry and molecular modeling, J. Ind. Eng. Chem. 72 (2019) 364–373, https://doi.org/10.1016/j.jiec.2018.12.038.

[54] A. Krzyzaniak, B. Schuur, A.B. De Haan, Equilibrium studies on lactic acid extraction with N, N-didodecylpyridin-4-amine (DDAP) extractant, Chem. Eng. Sci. 109 (2014) 236–243, https://doi.org/10.1016/j.ces.2014.01.030.

[55] H. Taymaz-Nikerel, E. Jamalzadeh, A.E. Borujeni, P.J.T. Verheijen, W.M. Van Gulik, S.J.J. Heijnen, A thermodynamic analysis of dicarboxylic acid production in microorganisms, in: Biothermodynamics Role Thermodyn. Biochem. Eng., Presses Polytechniques Et Universitaires Romandes, 2013: pp. 547–579. https://doi.org/10.1201/b15428-28.