Low-waste fermentation-derived organic acid production by bipolar membrane electrodialysis—an overview

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Abstract

Organic acids, e.g. citric acid, fumaric acid, lactic acid, malic acid, pyruvic acid and succinic acid, have important role in the food industry and are potential raw materials for the sustainable chemical industry. Their fermentative production based on renewable raw materials requires innovatively designed downstream processing to maintain low environmental impact and resource efficiency throughout the production process. The application of bipolar membranes offers clean and effective way to generate hydrogen ions required for free acid production from its salt. The water dissociation reaction inside the bipolar membrane triggered by electric field plays key role in providing hydrogen ion for the replacement of the cations in organic acid salts. Combined with monopolar ion-exchange membranes in a bipolar membrane electrodialysis process, material flow can be separated beside the product stream into additional reusable streams, thus minimizing the waste generation. This paper focuses on bipolar membrane electrodialysis applied for organic acid recovery from fermentation broth.

Keywords Alkali recycling · Downstream process · Electromembrane process · Organic acid recovery

Introduction

The preference toward renewable and bio-based chemicals is higher and higher nowadays, and this fact encourages and inspires scientists to develop and fine-tune biotechnological organic acid production. The key focus of research is on the reduction of raw material costs (Dörsam et al. 2017; Sawant et al. 2018), on the optimization of microorganisms (Yin et al. 2015; Johansen 2017; Li et al. 2021), yield (Liu et al. 2017), and last but not least recovery methods (López-Garzón and Straathof 2014).

Organic acids are produced industrially by either fermentation or chemical synthesis (Pinazo et al. 2015). The main advantage of synthesis is that the resulting product is usually of high purity and concentrated (Ai and Ohdan 1997; Gao et al. 2018). But the high energy demand and the use of expensive catalysts (Sang et al. 2019), in some cases toxic, environmentally hazardous reagents (Prikaznov et al. 2011; Solmi et al. 2019), represent great shortcomings of synthetic

methods. Microbial cell factories work under mild conditions in aqueous solutions. The main drawback of fermentation is the recovery of the product from a complex matrix. Innovative techniques, however, can overcome that hurdle.

Several membrane-based processes have proven effective in the extraction of valuable materials from complex matrices (Castro-Muñoz et al. 2018; Stoller et al. 2018). The experience gained in membrane technology for the treatment of industrial and agricultural wastewater can also be applied to the fermentation industry. Among others, bipolar membrane electrodialysis has been successfully used to treat industrial wastewater with high salinity (Tian et al. 2019).

Bipolar membrane electrodialysis (ED-BPM) is a promising technique for the recovery of bio-products that exist in ionic form in a certain pH range. Since supplementary substances for organic acid recovery are not required—unlike the traditional process—there is even the possibility to recycle the separated aqueous process streams in biotechnological procedures that are sensitive to chemical load.

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Acids in the scope of this study

The physicochemical properties of organic acids vary with the number of carbon atoms, carboxyl groups, or additional functional groups like oxo- or hydroxy substituents (Rawn and Ouellette 2018). Hereby, we present a selection of organic acids of food significance, among which mono-, di- and tricarboxylic acids, oxo- and hydroxyl-acids, saturated and unsaturated acids also can be found. These represent a broad variety of organic acids having significance or potential in the large scale chemical industry as well (Aurich et al. 2012).

Pyruvic acid also referred to as 2-oxo-propanoic acid has gained interest in the food industry as a potential fat burner that can accelerate the fatty acid metabolism in humans in the form of calcium pyruvate (Stanko et al. 1992). Special diets supplemented with pyruvic acid result in improved leg exercise endurance (Stanko et al. 1990), and lower cholesterol (Stanko et al. 1994). It is also a valuable substrate for the enzymatic production of amino acids such as L-tryptophan, L-tyrosine, and L-dihydroxyphenylalanine (L-DOPA) (Li et al. 2001).

Lactic acid (2-hydroxy-propanoic acid) is used in the food industry as a preservative, pH regulator, and taste-enhancing additive (Bai et al. 2003). Lactic acid-producing microorganisms are capable to form lactic acid from pyruvate.

Citric acid or 2-hydroxypropane-1,2,3-tricarboxylic-acid is used extensively in carbonated beverages to provide taste and complement fruit and berry flavors. It also increases the effectiveness of antimicrobial preservatives. Over 99% of the citric acid produced worldwide is the result of fermentation processes (Berovic and Legisa 2007).

Succinic acid (butanedioic acid) is produced both synthetically and via fermentation. Succinic acid of biotechnological origin is used in the food industry as an acidulant, as a flavoring agent, and as an antimicrobial agent. Furthermore, fermentation-derived succinic acid has the potential to become a large-volume commodity chemical (Zeikus et al. 1999).

Fumaric acid (trans-butenedioic acid) is a four-carbon dicarboxylic acid that is 1.5 times more acidic than citric acid. Therefore, it is commonly used as a food acidulant and beverage ingredient. Additionally, fumaric acid is widely used in the feed industry as an antibacterial agent and a physiologically active substance. It is also a valuable intermediate in the preparation of edible products, such as L-malic acid and L-aspartic acid. With the increasing market share of L-aspartic acid and L-malic acid in sweeteners, beverages, and other health food areas, the worldwide demand for fumaric acid and its derivatives grows each year (Xu et al. 2012).

Malic acid (2-hydroxybutanedioic acid), just like succinic acid and fumaric acid, is a four-carbon dicarboxylic acid and an intermediate in the citric acid cycle. As it possesses a greater acid taste and better taste retention than citric acid, malic acid is mainly used as an acidulant and flavor enhancer in beverages, candy, and food. It can be produced enzymatically from fumaric acid or biosynthetically from carbohydrates via fermentation (Chi et al. 2016).

Some important physical and chemical properties of the above-listed acids can be found in Table 1.

Fermentation processes for organic acid production

Organic acid production by microorganisms is related to their carbon source catabolism and energy management (Sanchez and Demain 2008; Trchounian and Trchounian 2019). Simple sugars can be used as carbon sources. Polysaccharides, primarily starch and cellulose are good substrates for acid production but generally, hydrolysis must be integrated into the process beforehand (Carta et al. 1999; Passoth and Sandgren 2019). Glycolysis is the first step in the breakdown of glucose to extract energy for cell metabolism. Pyruvate formed at the end of glycolysis may enter the citric acid cycle if it is present in the cell. The intermediates of the citric acid cycle are organic acids like citric acid, succinic acid, malic acid, etc. (Kertes and King 1986). Metabolic evolution resulted in potential organic acid overproducing microbial strains from various natural habitats (Sanchez and Demain 2008).

In the last century, labor and time-consuming efforts have been taken to screen microorganisms for the overproduction of organic acids for future industrial applications (Yu et al. 2020). The screening work was successful in many cases, and potent wild-type strains were collected and preserved in strain deposits. The understanding of the metabolic pathways, the genetic background and regulation behind them led to novel, high-performance screening techniques, that accelerated the efficiency of finding new efficient strains,

Table 1 Physical and chemical properties of organic acids in the scope of this study

Acid name	Solubility in water at 20 °C (g/L)	pK _a values	Melting point (°C)
Citric acid	592	3.14; 4.77; 6.39	153
Fumaric acid	4.9	3.03; 4.54	287
Lactic acid (DL)	Miscible	3.86	18
Malic acid (DL)	558	3.40; 5.11	128–132
Pyruvic acid	Miscible	2.50	12
Succinic acid	58	4.16; 5.61	185–190

even from a large number of genetically modified mutants (Sanchez and Demain 2008; Yin et al. 2015).

For the biotechnological production of organic acids, three possible implementations are given (Li et al. 2001):

- direct fermentation method;
- resting cell method;
- enzymatic method starting from a precursor.

At the end of all the processes, acids are usually present in an aqueous solution with a 5–20w% concentration.

Glucose is a basic carbon source in organic acid fermentation research. In Table 2, we collect some effective microorganisms that have great potential in industrial organic acid production, and we have indicated the achievable broth concentration in direct fermentation processes carried out with them, starting from glucose.

The application of bacteria, yeasts or filamentous fungi together with the complex nitrogen and carbon sources in the fermentation medium greatly influence the rheological properties of the broth from which recovery has to be performed (Charles 1978; Dhillon et al. 2013).

The pH of the fermentation and type of base used in the process are also of interest, as they can determine which recovery methods can be used, how the steps of the process can be integrated and whether or not side streams can be recycled. For example, ammonia, sodium hydroxide or potassium hydroxide can be recovered by bipolar membrane electrodialysis (Molnár et al. 2010; Xue et al. 2015; van Linden et al. 2020), whereas calcium carbonate cannot be.

The optimization of fermentation processes has to support a feasible product recovery to become an alternative for chemical synthesis.

Downstream processing of fermentation media

Downstream process is a sequence of separation processes applied to purify specialty chemicals such as organic acids from biotechnological production (Whittington 1990). Organic acids in the scope of this study are produced as extracellular metabolites. Their recovery therefore typically involves the following functions (López-Garzón and Straathof 2014):

1. Clarification: removal of large particles, microbial cells, and their debris.
2. Primary recovery: separation of the product from bulk aqueous solution and from major impurities.
3. Counterion removal: replacement of the cation of organic acid salt by H^+ to get carboxylic acid (if required).
4. Concentration/purification: partial removal of the solvent achieving concentration; removal of remaining impurities.

Figure 1 shows possible downstream processing sequences.

Clarification and concentration include classical methods in all direct fermentation processes. Clarification is usually accomplished by centrifugation or microfiltration (Whittington 1990; Gryta and Tomczak 2015), or a combination of the two methods, whereas concentration means solvent evaporation by distillation or crystallization (Gryta and Waszak 2016; Karp et al. 2018). They give a frame to downstream operation: the first step is the separation of

Table 2 Some organic acid overproducing strains, and product concentration at the end of direct fermentation—the listed strains utilized glucose as carbon source in the indicated fermentations

Organic acid	Producing strain	Organic acid concentration in the fermentation broth	Reference
Pyruvic acid	recombinant <i>Escherichia coli</i>	62 g/L	(Zelić et al. 2003)
	<i>Torulopsis glabrata</i> IFO 0005 multiauxotrophic yeast	67.8 g/L	(Miyata and Yonehara 1996)
Lactic acid	<i>Lactobacillus casei</i> LA-04–1	112.5 g/L	(Ding and Tan 2006)
	<i>Corynebacterium glutamicum</i>	95 g/L	(Okino et al. 2005)
	<i>Rhizopus oryzae</i> NRRL 395	60 g/L	(Bulut et al. 2004)
Citric acid	<i>Aspergillus niger</i> PM1	121 g/L	(Papagianni et al. 1999)
	<i>Candida lipolytica</i> Y1095	78.5 g/L	(Rane and Sims 1993)
Succinic acid	<i>Actinobacillus succinogenes</i> ZT-130	33.8 g/L	(Corona-González et al. 2008)
	<i>Anaerobiospirillum succiniproducens</i> ATCC 29,305	35.2 g/L	(Lee et al. 1999)
Fumaric acid	<i>Rhizopus arrhizus</i> NRRL 1526	38 g/L	(Riscaldati et al. 2000)
	<i>Rhizopus oryzae</i> ATCC 20,344	37.2 g/L	(Zhou et al. 2002)
Malic acid	<i>Aspergillus oryzae</i> NRRL 3488	30.2	(Knuf et al. 2013)
	<i>Escherichia coli</i> XZ658	34 g/L	(Zhang et al. 2011)

Fig. 1 Downstream processing sequences for the recovery, purification, and upgrading of fermentative carboxylic acids (CED = conventional electrodialysis; ED-BPM = bipolar membrane electrodialysis)

cell mass and solids, and the last step, the removal of the solvent to get a concentrated or solid product from its pure solution. The steps between the two can vary widely. The challenge is to get rid of the complex soluble matrix—with as much recycled substance as possible to minimize waste and new material need, and to apply the desired counterion in the product (special salt or acidic form). The recovery process should be tailored for the organic acid in question to achieve the optimum result.

Primary recovery of organic acids

After the clarification of fermentation broth, the filtered carboxylate solution still contains numerous impurities such as sugars and salts remaining from the fermentation feed, and fermentation by-products, such as proteins and undesired carboxylic acids, secondary metabolites. In all recovery strategies, the bulk of the impurities are removed by selectively transferring the product to another phase.

The oldest technique to realize primary recovery is precipitation. For example, citric acid, the first organic acid produced on a large scale by fermentation, is precipitated from the clarified broth with the addition of calcium hydroxide in a classical industrial plant. The formed insoluble calcium citrate can be thus separated from bulk water and impurities (Wang et al. 2020). The precipitate is filtered off and washed. The next step is acidification using sulfuric acid which yields soluble citric acid and a large amount of gypsum as a by-product. Only the precipitation method cannot be applied in all cases. Although the calcium salt of pyruvic

acid, for instance, is poorly soluble in water, the instability of pyruvate under alkaline conditions hinders the applicability of precipitation (Li et al. 2001). A well-designed process for the primary recovery of pyruvic acid is a distillation process with high energy costs. The alternative possibilities for precipitation are solvent extraction, ion exchange, and electrodialysis (ED).

Conventional electrodialysis

Electrodialysis is an electromembrane process. The key components of that process are ion-exchange membranes. The particular role of ion-exchange membranes is to transport and separate ionic components selectively (Strathmann et al. 2013). Regarding their function, they are classified as:

- cation-exchange membranes—that contain fixed negatively charged ions, thus having a selective permeability for cations;
- anion-exchange membranes—they are enriched with fixed positively charged ions, and have a selectivity for the transmission of anions;
- bipolar membranes—which consist of a cation- and an anion-exchange membrane laminated together, the close proximity of the fixed opposite charged ionic ligands creates a special interfacial interaction, that promotes water dissociation under low electric voltage.

Separation by electrodialysis is based on the ionic state of carboxylic acids in a certain pH range. By using ion-selective membranes in electric field, the carboxylate anion is recovered from fermentation broth while large molecules and solutes with opposite charge or no charge at all are retained. The pH of the feed solution should be adjusted to the experimentally determined optimum of electroseparation (Novalic et al. 1995).

The transport of an ion through an ion-exchange membrane or within an electrolyte solution occurs under the driving force of the electrochemical potential gradient of the ion, which is a function of the electrical potential and the chemical potential. Chemical potential shows dependence on the given species, the activity of the species, temperature, and pressure (Strathmann et al. 2013). The charge number of the ion also influences the migrating driving force; hence, in the case of di- and tri-acidic organic acids, the pH is of special interest. Direct current is used to create electric potential difference on the two sides of the membranes.

The conventional electrodialysis (CED) is a reliable process for more than half a century for primary recovery and concentration application. A conventional electrodialysis unit consists of a series of alternating anion- and cation-exchange membranes arranged between two electrodes. When electrical potential difference between the electrodes

is established, the anions migrate toward the anode. They are able to pass through the anion-exchange membrane but are retained by the cation-exchange membrane. The cations move in a similar but countercurrent way. The overall result is that an electrolyte is concentrated in alternate compartments while in the other compartments ions are depleted. Experiments for pyruvic acid (Zelić and Vasić-Rački 2005), lactic acid (Bailly et al. 2001), citric acid (Novalic et al. 1995), and succinic acid (Glassner et al. 1995) with CED primary recovery have been performed showing general applicability of the method. In the case of malic acid, conventional electrodialysis was tested to recover it as a by-product from an industrial fermentation process involved in the manufacturing of alcoholic beverages and proved to be effective (Lameloise et al. 2009). Enzymatic conversion of fumaric acid to L-malic acid was successfully integrated with CED to selectively recover malic acid from the reaction solution, after the precipitation and recycling of the remained fumaric acid (Bélafi-Bakó et al. 2004). Though references for CED as a recovery process for fumaric acid are scarce, another integrated technique for ammonium-L-malate production from ammonium-fumarate (Sridhar 1988) gives some clues that a CED process for primary recovery could be implemented for fumaric acid as well.

Counterion removal

In optimized fermentation processes, pH is usually one of the key parameters. The applied pH range varies for each microorganism, but life phenomena can be considered inhibited below pH 2 (Sharma et al. 2016) and above pH 12–13 (Preiss et al. 2015) with some rare exceptions. Due to the weak acidity of the organic acids in question, there is a certain degree of dissociation i.e., salt formation even in a fermentation performed at low pH. In the final product, the metal ion content is usually regulated by quality standards and regarded as an impurity. The efficiency of the applied technology for replacing counterions with hydrogen greatly influences the quality of the produced organic acid.

In precipitation—being the classical primary recovery technique for organic acids—classical counterion removal is the displacement of the organic acids from their insoluble salts by a strong acid. The chosen acid shall form another insoluble salt with the cation, Ca^{2+} or Mg^{2+} in general (López-Garzón and Straathof 2014) while the free acid becomes a solute. Sulfuric acid is the most cost-effective inorganic acid for the purpose. The inorganic salt by-product, e.g., gypsum, is formed in comparable quantities as the product itself. In the case of weakly soluble acids, e.g., fumaric acid, the operating temperature of acidification is high to keep the free acid in dissolved state while the inorganic precipitate is filtered off (Xu et al. 2012); thus, in

addition to by-product formation, the energy consumption is high, too.

All in all the recognition of the water dissociation catalyzing behavior of bipolar membranes under electric voltage (Frilette 1956) gave an advantageous possibility to provide the hydrogen ions from pure water, as scientists have recognized it at the outset of the research on it (Nagasubramanian et al. 1977). Recently, the development of ion-exchange membranes concerning their chemical and mechanical resistance shifted the focus from basic research to industrial usability.

Bipolar membrane electrodialysis

Industrial bipolar membrane electrodialysis technologies are already available for industrial wastewater treatment to valorize aqueous salt streams—either organic or inorganic—by generating acidic and caustic by-products. Being an additive-free possibility to influence the pH of an aqueous solution, the food industry utilizes specially designed types of ED-BPM equipment for adjusting the acidity of edible fluids (specifically sugar syrups, fruit and vegetable juices, wines, sauces, and tomato paste) (Bazinet et al. 1998). To inhibit undesired enzymatic reactions—e.g., the enzymatic browning of cloudy apple juice—the process is also in use. Shifting the pH from the enzyme-optimum in the highly acidic range causes partial, irreversible denaturation of the enzyme thus activity loss; then, the pH is readjusted to the original value in the same equipment but another cell stream. The treatment enhanced the color of cloudy apple juice during storage without modifying the flavor (Tronc et al. 1998).

Industrial ED-BPM organic acid production plants have been first established in 1995 in the USA, and several others followed in Japan and Europe (Bailly 2002). Those, however, use organic acid salts of high purity as raw material for acidification.

The main cost of membrane-based processes is the membranes themselves and the specific energy requirement (Castro-Muñoz et al. 2018). The recent results of membrane development should be taken into account in the industrial implementation, thus the maintenance costs (Zhao et al. 2021b), energy demand (Yan et al. 2018) and product purity (Liao et al. 2020; Yan et al. 2020) can be beneficially affected. Specific energy consumption from experimental results, however, can be taken as an indicator of the economic viability of the process (Zhao et al. 2021a).

A theoretical calculation was carried out by Wang et al. to determine whether ion exchange or bipolar electrodialysis is the economically better choice for counterion removal in the production of gluconic acid as a model organic acid (Wang et al. 2011). They introduced two factors into their calculations: an environmental factor and a membrane factor. Their results show that the ion-exchange

process is more economical when environmental considerations are less important. However, when this factor increases in a medium range, the combined ion exchange-electrodialysis system is more advantageous. According to Wang et al., bipolar membrane electrodialysis will become truly competitive when environmental costs rise and bipolar membrane prices fall.

The performances of the ED-BPM process can be evaluated in terms of the specific energy consumption (kWh kg^{-1}), the recovery rate of the organic acid (%) and the average current efficiency (%). The detailed calculation method is described in (Sun et al. 2017).

Organic acids can be produced directly from clarified fermentation medium by ED-BPM. Compared to the processing of an organic acid solution from primary recovery process, more significant membrane fouling may occur in such cases. The cell-free solution contains several different anions, and the effect of their presence on the recovery of fumaric acid was investigated in one-, two- and three-component model solutions at different current densities (Prochaska and Woźniak-Budych 2014). The other anions were present in an order of magnitude lower concentration than the fumarate ions, but the recovery rate was still significantly reduced at lower current densities, especially in the case of tertiary model solution with acetate and chloride ions. Comparing data from the fumarate-acetate binary model solution and the fumarate-acetate-chloride tertiary model solution, it was interesting to observe that while the recovery ratio of fumaric acid was reduced by one-third in the tertiary solution compared to the binary solution, the recovery ratio of acetic acid was not affected significantly by chloride ions. In the same study, the ED-BPM of fermentation broth pretreated with nanofiltration was investigated. In addition to fumaric acid, cordycepic acid and glycerol as a substrate for bioconversion were present in this broth. The bipolar electrodialysis was not selective for fumaric acid and cordycepic acid, but retained glycerol almost completely in the diluate stream. In another research, Kim et al. demonstrated that a single-step ED-BPM procedure may be more suitable than the two-step CED + ED-BPM recovery method of lactic acid directly from microfiltered fermentation broth (Kim and Moon 2001). A three-chamber arrangement was found to be suitable for this purpose, provided that a properly selected cation- and anion-exchange membrane is used.

In Table 3, some promising results are presented for organic acid recovery using a model or real fermentation broth feed. However, in the majority of the works listed in which real fermentation broth has been tested, the ED-BPM technique is applied primarily as a counterion removal step after a partially purifying/concentrating CED pretreatment.

The following cell configurations have been tested (Fig. 2).

- Two compartments with cation-exchange and bipolar membranes where soda is removed from the salt compartment through the cation-exchange membrane (CEM-BPM).
- Two compartments with anion-exchange and bipolar membranes where the acid is removed from the salt compartment through the anion-exchange membrane (AEM-BPM);
- Three compartments anion-exchange, cation-exchange, and bipolar membranes where the organic acid and the counterions are removed from the salt compartment through the anionic and cationic membrane, respectively (AEM-CEM-BPM).

These configurations are fundamentally different. In a CEM-BPM process, the salt stream is fed between the CEM side of the BPM and the CEM, and only the cations have to be transported through a membrane. This process is only adequate if the acid salt is in a pure solution and the goal is to produce free acid (Fig. 2a). The pure alkaline solution obtained on the concentrate side can be used for pH control in fermentation, as it was demonstrated in an integrated continuous lactic acid fermentation-ED system (Wang et al. 2013).

In an AEM-BMP process, the organic acid anions have to pass through the anion-selective membrane, the salt stream is fed between the AEM side of the BPM and the AEM. The anions pass through the anion-selective membrane and combine with the H^+ generated on the CEM side of the BPM. This method gives a possibility to get rid of impurities in the feed stream. If the AEM and the separation parameters are chosen carefully also anionic impurities of some kind can be removed (Fig. 2b). When the concentration of organic acid anions becomes low enough, the BPM-generated hydroxide ions start migrating through the anion-exchange membrane. In the acidic concentrate compartment, they recombine with hydrogen ions to water. This futile phenomenon reduces the current efficiency and thus limits the increase in the recovery rate (Kim and Moon 2001).

In the three-compartment configuration, both the acid anions and the cations must pass through a membrane (Fig. 2c). That increases the necessary energy input for operation, but it should be mentioned that there are two product streams if we consider that an uncontaminated alkali solution is generated simultaneously which can be recycled into the fermentation process as in the CEM-BPM configuration. In that case, the leakage of water ions is inhibited due to the membrane arrangement.

In a study on pyruvic acid recovery, the three-compartment ED-BPM was tested on model solution and two, differently pretreated real fermentation broths (Zelić and Vasić-Rački 2005). The ED-BPM with cell-free fermentation broth performed poorly compared to ED-BPM with

Table 3 Collected data on ED-BPM experiments performed on model solutions or real fermentation broth

Organic acid	Reference	Source of salt solution	Broth concentration	Recovery rate by ED-BPM	Current efficiency	Specific energy consumption	ED-BPM configuration
Pyruvic acid	(Zelić and Vasić-Rački 2005)	recombinant <i>E. coli</i> YJC202 clarified fermentation broth	41 g/L	60.2% (cell-free broth) 84.3% (cell and protein-free broth)	> 90%	1.5 kW·h·kg ⁻¹	AEM-CEM-BPM
Lactic acid	(Hřová et al. 2004)	<i>Lactobacillus plantarum</i> L10 clarified fermentation broth	171 g/L (preconcentrated solution using conventional ED)	95% (ultrafiltered, multivalent metal ion free broth)	79%	0.95 kW·h·kg ⁻¹	CEM-BPM
	(Timbuntam et al. 2008)	<i>Lactobacillus rhamnosus</i> clarified fermentation broth	117 g/L	80%	52.3%	1.91 kW·h·kg ⁻¹	AEM-CEM-BPM
	(Li et al. 2009)	fermentation broth	100.25 g/L	81.2%	91.8%	0.81 kW·h·kg ⁻¹	AEM-CEM-BPM
	(Madzingaidzo et al. 2002)	ultrafiltered fermentation broth	148.94 g/L (sodium salt)	71.2%	99%	0.605 kW·h·kg ⁻¹	AEM-CEM-BPM
	(Kim and Moon 2001)	microfiltered broth from a continuous cell-recycling fermentation process	79.4 g/L	98.7%	83%	1.4 kW·h·kg ⁻¹	AEM-CEM-BPM
Citric acid	(Tongwen and Weihua 2002)	model solution of sodium-citrate	0.5 mol/L	–	65–95%	3–8 kW·h·kg ⁻¹ (average data not shown)	AEM-CEM-BPM
	(Sun et al. 2017)	model solution of sodium-citrate	3.3%	97.1%	73.7–100%	5.88 kW·h·kg ⁻¹	AEM-CEM-BPM
	(Novalic et al. 1996)	model solution of sodium-citrate	10% (acid)	–	55–75%	2.08–6.11 kW·h·kg ⁻¹ (determined under different current densities)	AEM-CEM-BPM
Succinic acid	(Fu et al. 2014)	model solution of sodium-succinate	0.5 mol/L	–	90%	2.3 kW·h·kg ⁻¹	AEM-CEM-BPM
	(Szczygiel et al. 2017)	clarified post-fermentation broth from glycerol-to-succinate bioconversion	43 g/L	47%	–	4.88 kW·h·kg ⁻¹	AEM-BPM
Fumaric acid	(Woźniak and Prochaska 2014)	<i>Rhizopus sp.</i> protoplast clarified fermentation broth	2.0 g/L	53.3%	85%	7.0 kW·h·kg ⁻¹	AEM-BPM
	(Prochaska and Woźniak-Budych 2014)	<i>Rhizopus sp.</i> protoplast clarified fermentation broth started from glycerol	2.78 g/L	40%	67%	7.3 kW·h·kg ⁻¹	AEM-BPM

Table 3 (continued)

Organic acid	Reference	Source of salt solution	Broth concentration	Recovery rate by ED-BPM	Current efficiency	Specific energy consumption	ED-BPM configuration
Malic acid	(Liu et al. 2014)	model solution of sodium-L-malate	0.3 mol/L	76.7%	70%	0.34 kWh kg ⁻¹	AEM-CEM-BPM (integrated in MEDCC)
	(Lameloise and Lewandowski 2012)	beverage industry waste water	23.93 g/L	93–97%	–	1.81–1.96 kWh kg ⁻¹	CEM-BPM

model solution. The recovery ratio was 30% lower, the specific energy consumption was 10% higher, though current efficiency was only slightly reduced. The underperformance was due to the effect of biological substances—such as proteins and cell debris—in the broth. This is supported by the fact that the results of the experiment with similar but ultra-filtered fermentation broth, the performances were comparable with those obtained with model solutions.

Timbuntam et al. (Timbuntam et al. 2008) compared the three ED-BPM configuration for lactic acid separation. According to their findings, the AEM-BPM gives the highest current efficiency and the lowest energy consumption. The use of a size-exclusion anion-selective membrane (PC 100D, PCA GmbH, Germany) prevented the permeation of negatively charged higher molecular weight metabolites and of other substances with no charge, e.g., carbohydrates along with the obvious retention of positively charged substances.

In contrast, Kim et al. (Kim and Moon 2001) found that a three-compartment ED-BPM was the most effective configuration for lactic acid recovery. They also compared the three configurations, but went further and checked the performances of different ion-exchange membranes.

The three different configurations were tested for citric acid production too (Tongwen and Weihua 2002), and it was stated that for citric acid recovery the CEM-BPM variant is the optimal choice. The use of three-compartment version for citrate acidification was found to be particularly costly, but it should be noted that the results shown here were obtained with just one production cell between electrode compartments. For a ED-BPM stack with many production cells, the exact values for energy consumption and current efficiency may be changed due to the cell number.

In the study on succinic acid recovery, three-compartment ED-BPM performed better than two-compartment variants reaching the highest current efficiency and moderate specific energy consumption (Fu et al. 2014).

For fumaric acid recovery from real fermentation broth, the AEM-BPM and CEM-BPM configurations were tested and it was concluded that the AEM-BPM process fits for the purpose (Prochaska and Woźniak-Budych 2014).

Malic acid was successfully recovered from model solution applying a CEM-BPM ED stack with high acid recovery ratio and acceptable specific energy consumption (Lameloise and Lewandowski 2012). However, similar experiments using real solution—a concentrate from CED of an alcoholic fermentation waste water stream—specific energy consumption significantly increased by 50% because of the presence of anionic impurities.

The key components determining the efficiency of the electrodialytic recovery process are the applied membranes. In laboratory research dedicated to analyze organic acid recovery from a production method, the possibility is not necessarily given to choose from a wide range

Fig. 2 Different ED-BPM configurations tested for organic acid recovery from fermentation broth

of ion-exchange membranes. The appropriate decision is generally the purchase of commercially available products. The use of Neosepta membranes by Astom Corporation (previously named Tokuyama) is widespread in research (Novalic et al. 1996; Madzingaidzo et al. 2002; Hřová et al. 2004; Zelić and Vasić-Rački 2005; Timbuntam et al. 2008; Lameloise and Lewandowski 2012; Sun et al. 2017), and it is also worth mentioning the ion-exchange membranes from the ACS Ltd. (Zelić and Vasić-Rački 2005; Prochaska and Woźniak-Budych 2014; Woźniak and Prochaska 2014; Szczygiełda et al. 2017).

The overall productivity of the process could be enhanced with a coupled-research on membrane development with special regard to the selectivity of ion-exchange membranes. For example, Cybulski et al. (Cybulski et al. 2018) produced pyruvic acid successfully from glycerol and also obtained significant amounts of α -keto-glutaric acid as a by-product. Both acids are valuable, and their effective separation might be feasible with CED or ED-BPM by the reasoning above.

The most common base used for pH regulation during fermentation is sodium hydroxide, with the mobile mono-charged sodium cation. The divalent cations present in broth are mainly substrates for the producing microorganism and as such are represented in a definitely lower concentration compared to sodium. In a continuous fermentation process, the ion-depleted ED-BPM diluate stream containing carbohydrates and other substrates could be recycled, and the retention of divalent cations in that case could be beneficial. The CEMs are worth testing for divalent cation rejection (Kim and Moon 2001).

Through the bipolar membrane, ideally, no mass transport occurs. However, its electrical resistance plays a very important role in determining the operating costs. For a process to be operated at low energy consumption, membranes with low electrical resistance are required (Kim and Moon 2001). The contribution of the electric resistance of bipolar membranes is the highest to the overall resistance of the ED stack. The bipolar membranes got interest in substantially different application fields too since they can couple different pH environments into a single electrochemical device

(Oener et al. 2020). BPMs with an interfacial catalyst layer between the laminated AEM and CEM were found to have smaller electric fields at the interface compared to samples with no added catalyst. A comprehensive numerical simulation model showed that the damping of the electric field in BPMs with a catalyst layer is a result of a higher water dissociation product (H⁺/OH⁻) flux, which neutralizes the net charge density of the CEM and AEM layer (Yan et al. 2018).

In ED-BPM, some of the membranes are exposed to high alkalinity during operation. The chemical stability of membranes is also the subject of research (Bulejko et al. 2017) and has great importance in the safe and long-term applicability of ion-exchange and bipolar membranes.

Even with well-chosen membranes, fouling is a problem to be solved. The process design of ED-BPM is closely related to that of the conventional electrodialysis using the sheet flow stack design. In intermembrane space, the fluid is circulated at a high velocity. A turbulent flow could be advantageous, but this increases the energy input. The insertion of specially designed spacers in transmembrane cells leads to obstructions that result in a strongly eddying motion of the circulated fluids (Probstein et al. 1972); thus, the laminar film on the membrane surface becomes thinner, and fouling can be prevented. The thickness of spacers has an optimal range in which the mass transfer coefficient only slightly decreases (Káňavová et al. 2015).

Conclusions

Biotechnological processes are considered as sustainable ways, methods to produce organic acids on large scale and these products mean alternatives to widely used platform chemicals that originate currently from fossil sources. Application of bipolar membrane electrodialysis in the downstream processing operations eliminates the inorganic waste generation. Another beneficial property of the application is its integrability into effective primary commodity management.

Three possible operational configurations have been recognized depending on the types of monopolar membranes used in combination with the bipolar membrane. The two-compartment configurations, where only one type of monopolar ion-exchange membrane is used, result in an acidic and an alkaline stream. If the applied monopolar membrane is cation-exchange type, the process is appropriate for the counterion removal from pure salt solution combined with alkali regeneration. In the case of combination with anion-exchange membranes, the organic acid anion can be removed from its original solution selectively, and the pH of the diluate stream shifts in the highly alkaline range during operation. In the three-compartment configuration, three separate aqueous streams are produced: product solution containing the organic acid in acidic form, alkali solution containing the cations (generally sodium) and hydroxide ions, and the diluate stream in which neutral materials and ionic components with high molecular size are retained. The most effective utilization of substances can be achieved by the application of the latter configuration although its energy consumption is relatively higher.

The fact that experiments with real solutions are underperforming compared to tests with model solutions highlights the importance of these investigations. They can shed light on unpleasant phenomena and unexpected effects for which a solution strategy should be developed in future.

In future, an overview on the progress made in the development of bipolar membranes in different application areas may be desirable to consider their potential application in ED-BPM processes for organic acid recovery.

Well-designed and multidisciplinary research on the ED-BPM processes optimized for the recovery of organic acids directly from fermentation broth will certainly result in competitive industrial methods, with low energy consumption, a stable long-term operation, and with no significant membrane fouling. The environmental benefits of that processes are beyond question.

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Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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