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Separation of succinic acid from fermentation broth: Dielectric exclusion, Donnan effect and diffusion as the most influential mass transfer mechanisms

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A B S T R A C T

Nanofiltration can be used to separate succinic acid (SA) from other organic acids in a fermentation broth. However, commercial nanofiltration membranes can be insufficiently selective since some produced organic acids have similar molecular weights. SA production from biomass fermentation entails separation of succinic acid from the other concomitantly produced organic acids such as acetic acid, formic acid, pyruvic acid etc. In this study, five commercial nanofiltration membranes were tested for SA rejection and selectivity under dead-end and crossflow modes of SA recovery from selected synthetic solutions and a real fermentation broth. SA rejections up to 94.1 ± 1.5% and 95.5 ± 3.5% were observed for the synthetic broth and the fermentation broth, respectively. The SA fractions obtained in the retentate were nearly 70% and 60% for synthetic and fermentation broth, respectively. The highest rejections and SA fraction values were achieved with DK and NF270 membranes, which also showed the highest permeate flux. Model evaluation using the Donnan-steric pore model with dielectric exclusion (DSPM-DE) showed that 99% of the SA rejection occurs at the membrane interface and not inside the membrane. Based on the modelling, the most important mechanism affecting separation was dielectric exclusion at both sides of the membrane surfaces. Moreover, identified sensitive model parameters, i.e., pore dielectric constant (εpore), charge density (Xq) and pore radius (rp), were estimated through model fitting and were found to be highly correlated with significant variations. Finally, for the first time, a calibrated model with synthetic broth was successfully used to predict organic acids rejection for a real fermentation broth (with 12% and 3% prediction error for succinate rejection by NF270 and DK, respectively). Such prediction was achieved only by measuring organic acid concentrations in the fermentation broth and using the three sensitive parameters. Furthermore, the potential contribution of different transport mechanisms of SA was quantified for the first time.

1. Introduction

Succinic acid (SA) is an organic acid that can replace petroleum to produce several commercial products such as solvents and lubricants, synthetic resins and biodegradable polymers (polybutylene succinate and polyamides) as well as cosmetics, food additives and pharmaceuticals intermediates [1,2]. The most recent applications of SA are in the production of 1,4-butanediol, plasticizers and alkyd resins [2]. Though SA is historically a petrochemical refinery product, it has recently been efficiently obtained from the fermentation of many biomasses, including agricultural and industrial wastes [3].

The downstream of SA production accounts for more than 80% of the operating costs of the overall production process [4] and typically includes several technologies such as electrodialysis [5], ion exchange columns [6], crystallization [7] and extraction [8]. The SA separation and purification process can be divided in four major steps: (I) microbial cell removal, (II) concentration and clarification (protein removal), (III) SA separation and concentration and, (IV) purification and final crystal formation. Microfiltration and ultrafiltration have been efficiently used for step I and II [9] and a high degree of isolation of SA from pigments,
increase in energy costs [6]. Yield and purity largely depend on the SA amount of water that subsequently needs to be removed to separate SA. SA yield [10,12]. Furthermore, the higher the dilution, the higher the NF selectivity) can be achieved with increasing dilution only up to a and yield needs to be found. Higher SA yield and purity (due to higher optimize the process of SA separation tion there are two major challenges, namely selectivity and yield. To E. Mancini et al.

A good example is crude glycerol, which has been identified as top more sustainable and economic second-generation biomasses are lower. A. Kang and Chang [12], using the same membrane (NF45) and similar operating conditions as in the study of Khunnokwao et al. [10], reported SA rejection values of about 80% for mixed organic acids solution with 0.3 M sodium succinate (35.4 g L\(^{-1}\)). The low rejection values suggest that fermentation broth dilutions may still be necessary for second generation SA to achieve high SA rejection. Moreover, recent studies reported significant advantages of a continuous SA fermentation strategy over batch and fed-batch strategies [3,17]. This is of importance in view of the fact that continuous SA fermentation enables higher production rate but lower SA concentrations in the fermentation broth. Another key factor which influences the separation of SA by NF is solution pH. SA almost completely dissociates at pH values above 7.0 (pK\(_a\): 4.2; pK\(_{a2}\): 5.6) and at this pH, almost all the commercial NF membranes are also negatively charged and therefore the repulsion between succinate and the membrane is significant. Depending on the adopted separation strategy, NF can be used to concentrate SA in the permeate or to retain it in the retentate. By adjusting operating conditions like pH and dilution of the fermentation broth, SA can be collected in the permeate together with the other organic acids (rejecting pigments, proteins, and residual non-fermented sugars) or can be separated from the other organic acids in the fermentation broth.

The market price of SA depends on its purity which needs to be above 99% for SA to be used as a building material for polymers. The impurities that could interfere with polymerization must be below 0.05 mol% [7]. Studies on NF of synthetic solutions report rejections from 77% [18] to 92% and purities of up to 99.5% [10]. However, levels of purity from diafiltration in NF of fermentation broth may be significantly lower. A patent from DSM and Roquette investigated the use of two NF steps (a concentration phase and a diafiltration phase) to separate SA from fermentation broth and reported a final SA purity of only 88% of dry matter (DM) [6].

Mathematical modelling of NF has been extensively used to enhance understanding of the mechanism of separation processes inside the membrane and facilitate improving NF separation efficiency by optimizing operating parameters. Most of these models are based on the Nernst-Planck equation describing transport of ions inside the membrane [19]. Such models are also used to describe separation of organic compounds [20]. For SA, there is only one study that has investigated such model performance in multi-ion solutions in a ceramic NF membrane [21]. In a more recent work, the Maxwell-Stefan equation was used to describe SA permeation through NF membranes in binary and ternary solutions [22]. Most of the modelling studies on NF performance used simple salt solutions [20–23] and, to the best of our knowledge, there are no studies modelling the separation of SA from a real fermentation broth. In general, there is a lack of understanding on the mass transfer mechanisms of organic acids across NF membranes, and particularly on the relative contribution of each force to the overall mass transfer. Not enough is known about the performance of NF with both synthetic and real SA fermentation broths, including the behaviour with non-charged molecules, such as xylene, that have similar molecular weights to SA. Greater understanding of mass transfer mechanisms in NF is fundamental for proper control of the operating conditions and thus for the final quality of the product. Such understanding would help to improve the efficiency and performance of SA separation via NF at commercial scale. This work therefore attempts to investigate the following:

I. Screening in dead-end filtration mode of five commercial NF membranes based on their performance in separating SA or xylene in solution with different concentrations and pH values.
II. Study of organic acids rejection and NF selectivity for SA synthetic broths in crossflow filtration mode.
III. Study of organic acids rejection and NF selectivity for SA fermentation broth.
IV. Simulation of NF in crossflow using the Donnan-Steric Partitioning and dielectric exclusion model to better understand the separation mechanisms in NF.
V. Prediction of NF membrane performance with fermentation broth after model calibration from the synthetic solution experiments (forward simulation) and potential identification of desired membrane characteristics of an optimal NF membrane for efficient separation of SA from other organic acids by-products.

The work commenced with an initial screening of known commercial NF membranes in dead-end filtration using SA solutions. Next, membrane performance was compared with that of solutions of xylene that has a similar molecular weight to SA but without charges. The best performing membranes were then tested in crossflow filtration to mimic real industrial application. Finally, the data from crossflow filtration were used to study the mechanisms of separation and the relative contribution of the forces to organic acid mass transfer across NF membranes.

2. Materials and methods

2.1. Experimental set up, chemicals and procedures

All the membranes were pretreated by dipping them in 0.5% NaOH solution for 10 min to remove manufacturing preservatives (following the manufacturer recommendations), rinsed and then soaked in ultrapure water for at least 12 h. Water permeability (\(I_p\) – Table S1) was measured immediately before starting the experiment and until a constant permeability value was observed. Every experiment was conducted at a temperature of 21 ± 1°C. Since different pH conditions are tested in this study, the organic acids can be protonated or dissociated; therefore the abbreviations for the organic acids, e.g. SA, PA, FA etc. are used to indicate both the acid and the dissociated form, e.g. SA represents both succinic acid and succinate.

2.1.1. Dead-end filtration

The screening of the NF membranes was done with 50 ml dead-end filtration Amicon cells (filtration area 0.00134 m\(^2\)). Before use, each membrane was washed with ultrapure water and pre-compact at the
The experimental operating pressure of 0.4 MPa for a total of ≥ 45 min until the water permeability was constant. Each experiment was then performed in duplicate with two cells in parallel loaded with the same feed solution. The experiments were conducted at 0.4 MPa, 300 rpm stirring speed, until a volume reduction ratio (VRR) of 1.25 (eq. (1)) was reached, which means 5 mL of permeate was obtained from a 25 mL of starting solution. Permeate and retentate were then collected for analysis and the membrane was washed for 30 min at 0.4 MPa with ultrapure water to remove the external fouling. Finally, water permeability in post-filtration \( \left( I_{p,t} \right) \) was tested until a constant permeability value was achieved.

2.1.2. Crossflow filtration

Due to the common industrial application and the lower fouling problems, crossflow filtration was used instead of dead-end filtration to study the membrane performances with the synthetic and the fermentation broths. The crossflow module is a self-made unit as in Fig. 1 with a filtration area of 0.00425 m\(^2\). Before use, each membrane was pretreated as described in section 2.1 and then pre-compacted with ultrapure water at the experimental operating pressure of 0.8 MPa for a total of ≥ 45 min. The crossflow velocity was kept at 7.4 L h\(^{-1}\) and the transmembrane pressure (TMP) of 0.8 MPa was controlled by a Micropump® and the retentate valve. Both permeate and retentate were continuously recirculated into the feeding vessel, and for each experiment, multiple samplings were performed over time to ensure that system stability was reached. Each test was performed in triplicate, but the same membranes were used for different tests.

2.1.3. NF of synthetic solutions using dead-end and crossflow modes

To study the mechanisms of SA separation with NF, different SA solutions with different pH values were prepared and tested in both dead-end and crossflow filtrations (Table 1). The synthetic solutions had the same components but at three different dilutions. The weight fraction of the organic acids mimics a typical composition produced by *Actinobacillus succinogenes* [24]. The pH of each solution was adjusted using NaOH. Since xylose and SA have comparable molecular weights, xylose solutions with the same molarity as the SA solution were also used to investigate separation and filtration time with an uncharged molecule (Table 2). After each experiment with SA, the membrane was washed with deionized water for 15 min and then the \( I_{p,t} \) was measured. The same membrane was then used to test the xylose solution at the same pH as the SA solution previously tested. Each experiment with both SA and the xylose solutions was conducted at a VRR of 1.3 (eq. (1)).

2.1.4. Fermentation broth for NF separation

The fermentation broth was obtained from a glucose batch cultivation of *Actinobacillus succinogenes* according to Ferone et al. [25]. The medium composition contained 10 g L\(^{-1}\) glucose, 5 g L\(^{-1}\) yeast extract, 1 g L\(^{-1}\) NaCl, 0.2 g L\(^{-1}\) MgCl\(_2\)6H\(_2\)O, 0.23 g L\(^{-1}\) CaCl\(_2\)2H\(_2\)O. The fermentation was conducted for 12 h in a 2 L fermenter inoculated with 5% v/v *A. succinogenes* inoculum; the pH was maintained at 6.8 ± 0.01 with 5 M NaOH, and pure CO\(_2\) gas was injected from the bottom of the fermenter. The fermentation broth composition is shown in Table 1. The fermentation broth was centrifuged for 10 min at 7000 RFC with a Heraeus Multifuge X3 FR, Thermo Scientific, to remove microbial cells while the pH values were measured with a PHM 210 MeterLab.

2.2. Equations and statistics

2.2.1. Metrics for performance comparison

To compare the performance of membranes in dead-end and crossflow filtration, different metrics were used: volumetric reduction ratio (VRR), observed rejection (R), and selectivity (S). VRR is defined as:

\[
VRR = \frac{V_0}{V_r}
\]

where \( V_0 \) is initial feed volume and \( V_r \) is the retentate volume.

The observed rejection was calculated differently for dead-end and for crossflow. For dead-end, the observed rejection (R) was calculated taking into consideration concentration of the studied solutes in the starting feeding solution, while for crossflow the rejection was calculated based on the concentration of solutes in the retentate (measured at the end of the experiments). This was done to minimize potential sampling error with respect to fouling phenomena such as concentration polarization or gel layer formation, which are more severe in dead-end filtration. Fouling phenomena could cause uneven distribution of organic acids in the retentate solution column. The observed rejection was calculated based on equation (2):

![Diagram of the crossflow filtration system](image-url)

Fig. 1. Diagram of the crossflow filtration system used with the best performing membranes identified in the dead-end experiments. The system is equipped with a feeding vessel (a), a pump (b), a chiller (c), a cell with a membrane (d) and three flowmeters to measure and control fluxes in-flow (e\(_1\)), permeate flow (e\(_2\)) and retentate flow (e\(_3\)).
where \( c_i \) is the concentration of \( i \) in the permeate solution, \( c_i^f \) is the concentration of \( i \) in the feeding solution, and \( c_i^p \) is the concentration of \( i \) in the retentate.

The membrane selectivity performance was studied by the following equation (3):

\[
S_{i,SA} = \frac{c_{p,i}}{c_{f,i}} \cdot \frac{c_{p,SA}}{c_{f,SA}} = \frac{c_{p,i}}{c_{p,SA}} \cdot \frac{c_{f,SA}}{c_{f,i}} = \frac{1 - R_i}{1 - R_{SA}}
\]

where \( x \) is an organic acid or ethanol in the synthetic or fermentation broth, \( c_i \) and \( c_i^f \) are the concentration in the permeate and in the feeding solution, respectively, and \( R \) is the rejection.

The SA fraction in the retentate was calculated with equation (4):

\[
SA \text{ fraction} \% = \frac{c_{SA,retentate}}{\sum c_i} \times 100
\]

where \( c_{SA,retentate} \) is the concentration of SA in the retentate and \( c_i \) indicates the concentration of each organic acid and alcohol in the synthetic or fermentation broth.

All the statistical analysis for the experimental part were made using the OriginLab program (OriginLab Corporation, Northampton, Massachusetts), while for the simulation part MATLAB R2020b (MathWorks Inc, Natick, Massachusetts) was used instead. The statistically significant differences (\( p < 0.05 \)) in the organic acids rejection and separation factor values were identified with one-way ANOVA and the outliers were identified with Grubb’s test.

### 2.2.2. Model description

To describe mass transfer of ions through a nanofiltration membrane, the Donnan steric pore model with dielectric exclusion (DSPM-DE) was used [26,27,28]. This model is developed by extending the Donnan-Steric Pore Model (DSPM) [28-30] and, importantly, adding the effect of dielectric exclusion as a separate parameter. Bowen and Welfoot [27] demonstrated that this model could result in a more realistic charge density but also lead to better model fitting especially for divalent salts, which is also the case in this study for succinate. The DSPM-DE model has been extensively applied and investigated [19,31,32]. Briefly, in the DSPM-DE model, the transport of ions inside the membrane is driven by diffusion, convection, and electro-migration. These mass transport phenomena for \( i \)th ion \( c_i \) are described by the extended Nernst–Planck equation (5):

\[
J_i = -K_\psi d\overline{c_i} + K_i c_i J_i - \frac{z_i D_i f_i \psi}{RT} \frac{d\psi}{dx}
\]

where, \( J_i \) (\( \text{mol m}^{-2} \text{s}^{-1} \)) is the solute flux and \( J_p \) (\( \text{m}^3 \text{m}^{-2} \text{s}^{-1} \)) is the permeate volume flux which are measured during each experiment. \( D_i \) (\( \text{m}^2 \text{s}^{-1} \)) is the diffusion coefficient, \( z_i \) is the charge number of the ion and \( \psi \) (V) is the electric potential. \( K_\psi \) and \( K_i \) are the hindrance factor for diffusion and convection, respectively. Other parameters, such as \( R \) (7.314 J K\(^{-1} \text{mol}^{-1} \)), \( T \) (294 K) and \( F \) (9.64867×10^4 C/eq), are the ideal gas constant, absolute temperature and Faraday constant, respectively.

At the interface of the membrane in contact with the feed solution and the permeate, the separation is characterized by three mechanisms: steric hindrance, Donnan equilibrium and dielectric exclusion. The steric hindrance is related to the “sieve effect” of the membrane and the Donnan equilibrium accounts for ion partitioning due to Donnan potential. Dielectric exclusion is exclusion of ions due to difference between the dielectric properties of the bulk with the respective dielectric properties of the membrane pores. The equilibrium can be described for the feed-membrane interface (eq. (6)) and the permeate-membrane interface (eq. (7)). These equations allow calculation of ion concentrations at the inside surface of the membrane (\( c_{i,N} \) and \( c_{i,P} \))

\[
\frac{c_{i,N}}{c_{i,P}} = \frac{\gamma_{i,N} \phi_i \exp(-\frac{z_iF}{RT} \Delta\psi_{i,DN})}{\gamma_{i,P} \phi_i \exp(-\frac{z_iF}{RT} \Delta\psi_{i,DP})}
\]

where \( \gamma_{i,N} \) and \( \gamma_{i,P} \) are the ion concentrations just inside and outside of the membrane surface at the feed-membrane interface with corresponding activity coefficients \( \gamma_{i,N} \) and \( \gamma_{i,P} \) while the constant \( c_{i,N} \) and \( c_{i,P} \) are the ion concentrations just inside and outside of the membrane surface at the permeate-membrane interface with corresponding activity coefficients \( \gamma_{i,N} \) and \( \gamma_{i,P} \).
The terms on the right-hand side of equation (6) and (7) represent the activity coefficient ratio, the steric hindrance coefficient, dielectric exclusion (solvation energy) and Donnan potential at the interface. Other equations in the DSPM-DE model (not presented here) include feed-membrane mass transfer resistance, charge balance inside the membrane and electroneutrality conditions. The model used in this study is based on the model developed by Geraldes and Brites Alves [33], which includes a complete model description and numerical procedure. The model was set up by calculating the concentration of dissociated organic compounds based on the Henderson–Hasselbalch equation and recorded pH. The amount of sodium ions was then calculated to ensure electroneutrality conditions. The model included 100 discretization points (N = 100) with mesh expansion factor of 1.1. The mesh is refined in both membrane-solution interfaces. The DSPM-DE model includes many model parameters which require membrane characterization through complex fitting procedures that often require tedious experimentation using different electrolytes [34–36]. In this study, an alternative approach was pursued to evaluate the relative importance of model parameters on the model predictions (sensitivity analysis) and consecutively parameter estimation by model fitting.

2.3. Sensitivity analysis

A sensitivity analysis was performed using standardized regression coefficients (SRC) [37]. In this method, linear regression models are built by constructing a meta model using the Monte Carlo procedure. This meta model is a simple linear model derived from the original model. For the i th Monte Carlo simulation, j th output parameter and k th model output, this model has the form:

$$s_{yk} = b_k + \sum_{j=1}^{M} b_{jk} \theta_j + \epsilon_k$$  \hspace{1cm} (8)

where $s_{yk}$ is single valued of the output $y$, $b_k$ is the linear regression coefficient, $\theta_j$ is the input parameter, and $\epsilon_k$ is the error of regression model. This equation can be formulated in a standardized form by applying mean-centered sigma-scaling [38]:

$$\frac{s_{yk} - \mu_{yk}}{\sigma_{yk}} = \sum_{j=1}^{M} \beta_{jk} \frac{\theta_j - \mu_j}{\sigma_j} + \epsilon_k$$  \hspace{1cm} (9)

where $\mu$ is the mean and $\sigma$ is the standard deviation, and $\beta_{jk}$ is the standardized regression coefficient (SRC) of parameter $j$ on output $k$. The higher the magnitude of this coefficient, the higher the contribution of the parameter on the output. Positive $\beta$ indicates the parameter has positive influence, and negative $\beta$ indicates negative influence on the model output.

2.4. Analytical procedures

Organic acids (succinate, propionate, acetate, formate etc.) concentration in the synthetic solutions and in the fermentation broth were measured using High Performance Liquid Chromatography (HPLC) (Shimadzu). For the fermentation broth, alcohols were also analyzed. The chromatograph was equipped with a refractive index detector (RID) and an Aminex HPX-87H column (Bio-Rad). An autosampler injected 40 µl from each sample vial for a total run of 20 min/sample for the synthetic solutions and 43 min/sample for the vials with fermentation broth. The eluent (H₂SO₄ 12 mM) flowed at a constant rate of 0.6 mL min⁻¹ isothermally at 63 °C. Xylose concentrations were analyzed with ICS Dionex with a CarboPac PA20 column at 21 °C and for 23 min with 10 mM NaOH eluent.

3. Results and discussions

3.1. NF of succinic acid and xylose solutions

Two solutions containing SA were tested in dead-end filtration in five commercial NF membranes (Table S1). The succinate rejection for the solution at 0.43 M (50 g L⁻¹) was rather low in all tested membranes and for all tested pH values. Specifically, the highest succinate rejection was observed at pH 5 for all membranes and with similar values, except for DK (Fig. 2). Succinic acid rejection at pH 2.2 was also rather similar among the membranes and was below 10%. There was no significant difference between rejection at pH 7.0 and pH 5.0 in both NF270 and NTR7450. In contrast, TS40, DL and DK showed no succinate rejection at pH 7.0.

However, despite the low rejection across different pH values, the permeate fluxes decreased dramatically with increasing pH, from more than 20 L h⁻¹ m⁻² at pH 2.2 to less than 0.80 L h⁻¹ m⁻² at pH 7.0 (Fig. 2). This is presumably due to the specific interaction between the membrane and the dissociation status of SA under different pH values. This specific interaction clearly disappears when testing the filtration of a neutral molecule – xylose – whose rejection is exclusively driven by size exclusion at the same molar concentration (0.43 M) and solution pH as those of SA. Fig. 2 shows that there is no significant difference in both xylose rejection and permeate flux at different pH values. Therefore the decrease of the SA permeate flux with increasing solution pH could be attributed to phenomena associated with electromigration. An important electromigration force is the repulsion between the nearly completely ionized form of SA in solution at pH 7.0 and the negatively charged NF. Theoretically, this phenomenon should also cause an increase in succinate rejection. On the contrary, however, succinate rejection for solution at pH 7.0 is found to be the lowest for 3 out of the 5 tested membranes (Fig. 2). A potential explanation for this could be the Donnan effect caused by higher concentration of Na⁺ in the solutions at pH 7.0 compared with those at pH 2.2 and 5.0. About 32 g L⁻¹ NaOH was added to buffer the broth to pH 7.0, which is equivalent of 0.82 M of Na⁺ and almost double the moles of succinate. While Na⁺ can freely pass through the membrane, succinate is repulsed. However, to maintain the Donnan equilibrium, succinate must also pass through the membrane, leading to low SA rejection. Another reason for the low SA rejection could be the charge shielding effect of a high concentration of Na⁺ ions, resulting in a weaker charge repulsion between succinate and membrane. Regarding the permeate flux, the process of succinate migration is slow, and the osmotic pressure generated by the high succinate concentration on the feed side reduces the permeate flux. Another
phenomenon that could explain the low permeate flux is hydration of succinate. Hydration of the succinate molecule would create an agglomerate capable of making the free passage of succinate and water more difficult. The bonding between water and succinate could lower the permeate flux because the steric hindrance of succinate would be higher. Therefore there is a hydration energy barrier that would require additional energy to break up [39]. Regarding xylose rejection, Fig. 2 shows that xylose is rejected more than SA, which is due to the higher molecular weight (150.1 g mol\(^{-1}\)) of xylose [40] compared with that of succinic acid/succinate which has a molecular weight of 118.09, 117.09 or 116.09 g mol\(^{-1}\), depending on the dissociation level. According to the findings of Morthensen et al. [41], the rejection of xylose was due to size exclusion, but the Donnan effect together with the solution complexity, ionic strength and pH can significantly affect xylose rejection. With NF270, the xylose rejection values were reported to be from about 10 to more than 60%.

To study further the interaction between membrane, SA and pH, the same NF membranes were tested for SA at 5 g L\(^{-1}\) (0.043 M) solutions at pH 2.2 and 7.0. The resulting SA rejection values climbed from 10% to more than 90%, when changing from pH 2.2 to pH 7.0 (Fig. 3).

The highest absolute succinate rejection is from NF270 (94.1 ± 1.5%), followed by DL (91.1 ± 1.0%), DK (90.6 ± 1.3%) and TS40 (86.8 ± 5.9%) (Fig. 3). The difference between the succinate rejection observed for 5 g-SA L\(^{-1}\) solution at pH 7.0 compared with the SA rejection for 50 g-SA L\(^{-1}\) is remarkable. The succinate rejection from NF270 and NTR7450 is, respectively, 5.3 and 6.9 times more for the SA solution at 5 g-SA L\(^{-1}\) compared to that of 50 g-SA L\(^{-1}\), and up to about 170 times more than for TS40, DL and DK. This can be explained again by electromigration-associated phenomena, i.e. screening. A sufficiently high SA concentration and Na\(^{+}\), like for 50 g-SA L\(^{-1}\), can screen the negative charges on the membrane surface, hence weakening the repulsive forces [13]. Furthermore, the concentration difference in the 50 g-SA L\(^{-1}\) solution causes a much higher diffusion force than in the 5 g-SA L\(^{-1}\) solution. When the permeate fluxes are examined, the values observed for TS40, DL and DK are no different for the solutions at pH 2.2 (25.2 ± 0.9, 21.5 ± 1.3 and 24.0 ± 4.6 L h\(^{-1}\) m\(^{-2}\), respectively), while NTR7450 and especially NF270 show higher permeate flux values (35.0 ± 0.7 and 55.0 ± 6.4 L h\(^{-1}\) m\(^{-2}\), respectively). However, the difference in permeate flux values between the membranes drops with the SA solution at pH 7.0. Moreover, the flux decrease between the solution at pH 2.2 and pH 7.0 is 11 times higher for SA at 50 g-SA L\(^{-1}\) (Fig. 2) compared to at 5 g-SA L\(^{-1}\) (Fig. 3).

Since the water permeability values before filtration are similar to those after filtration (\(I_p = I_{p, f}\) – data not shown), no irreversible fouling occurred and the SA rejection is associated with electromigration-related forces, e.g. electrostatic repulsions (which are highest at pH 7.0). However, there is some rejection for the non-dissociated SA (pH 2.2) and this could be due to size exclusion. Therefore the different performances of the NF membranes are associated with specific membrane pore size, with type of membrane polymers (Table S1), and with membrane specific charge density [42].

### 3.2. Crossflow filtration of synthetic and fermentation broth

The membranes giving the highest absolute rejection performance in dead-end filtration, i.e. NF270, DL and DK, were further tested with the synthetic broths. The synthetic broths composition is reported in Table 1 and mimics the organic acids composition of the fermentation broth typically produced by *A. succinogenes* [24]. Along with the starting synthetic broth at 10 g-SA L\(^{-1}\), two dilutions were also tested (Table 1). For the 10 g-SA L\(^{-1}\) synthetic broth, the SA rejection from NF270 and DK was not statistically different (\(p > 0.05\)), but was statistically higher than SA rejection from DL (\(p < 0.05\)) (Fig. 4). For synthetic broth 5 g-SA L\(^{-1}\) and 3 g-SA L\(^{-1}\), the overall rejection of all organic acids decreased with increasing the concentration (Fig. 4), while for synthetic broth 3 g-SA L\(^{-1}\), only SA showed a positive rejection for all the tested membranes. Formic acid (FA) was “negatively rejected” in all scenarios, which means that FA is basically extracted from the feeding solution because of the Donnan effect. This could be due to the lower molecular weight of FA compared with the other organic acids in solution (Table S2).

With respect to the selectivity between SA and each of the other organic acids in solution, all NF membranes showed the highest absolute selectivity for FA over SA. However, the separation of SA from the other organic acids, i.e. \(S_{AA/SA} > S_{PA/SA} > S_{FA/SA}\) was not statistically significant (\(p > 0.05\)), except for DL (\(S_{PA/SA} > S_{FA/SA} = S_{AA/SA}\)) with synthetic broth 3 and 5 g-SA L\(^{-1}\) (\(p < 0.05\)) (Figure S2). Higher selectivity with dilution was also seen for DK but not statistically significantly for NF270 (\(p > 0.05\)). On average, the selectivity of DL for SA and each of the other organic acids in solution was the lowest among the tested membranes, but the smaller deviation among the values for DL may reflect a more homogeneous membrane structure (Figure S2). When DK with synthetic broth 3 g-SA L\(^{-1}\) is excluded, the succinate rejection and separation factor of NF270 are on average the highest among the tested membranes (Table 2).

Finally, the clarified fermentation broth was filtered using NF270 or
DK. The SA rejection was up to 95.5% with DK (Fig. 5), which was not statistically significantly different to SA rejection with NF270 (P > 0.05). Khunnonkwao et al. [10] achieved similar SA rejections of about 90% for SA concentration ≤ 0.07 M (8.3 g L⁻¹) in synthetic solutions at pH 7 with NF45 and for permeate fluxes from 2 to more than 3 times higher (11–18 L m⁻² h⁻¹) than those in our study. By contrast Lub sungneon et al. [18] studied SA separation from A. succinogenes fermentation broth using an NF (multi-channel ceramic) membrane, and reported less than 80% SA rejection for 10 g-SA L⁻¹ concentration at pH 6.5 and up to 0.4 MPa. Interestingly, Lub sungneon et al. [18] did not report much lower SA rejection values for much higher SA concentrations, and at 50 g-SA L⁻¹ and 0.6 MPa, the reported SA rejection was 83.3%. In comparison, in our study, about 10% higher SA rejection for A. succinogenes fermentation broth at 4.5 g L⁻¹ was achieved for NF270 and DK, respectively (Table 2, Fig. 5). However, considering all the organic acids and alcohols in the broth, the SA fraction achieved in our study was below 60% and 70% for the synthetic and the real fermentation broth, respectively.

NF of the clarified fermentation broth showed a clear enrichment of SA in the retentate, with rather similar performance by NF270 and DK (Fig. 5). The fermentation broth used in this work contained relatively high concentrations of formate and acetate. For both NF270 and DK, formate was clearly extracted (from the feeding solution), while acetate was slightly rejected. DK showed higher absolute selectivity performance with respect to each compound in solution, but no statistical difference was observed between the two membranes (Figure S1). Overall, NF270 can be considered the best membrane among those studied in this work for the rejection of SA, because it combines high permeate flux with high SA rejection and selectivity.

As can be seen in Figs. 4 and 5 and in Table 2, the behavior of NF270 and DK in rejecting common organic acids from the synthetic broth and from the fermentation broth is similar. This suggests that it might be possible to predict the performance of the NF membrane after model calibration with synthetic solutions and to study which mechanisms and parameters dictate the mass transport of organic acids across the membrane.

3.3. Separation mechanism: Donnan-Steric partitioning model

3.3.1. Sensitivity analysis

There are several parameters affecting the transport of the compounds across the membrane. A sensitivity analysis was performed to measure the sensitivity of model output to variations of the model parameters. The parameters considered are listed in Table 3. A linearized model for each analysis (average R² = 0.75) could be achieved with 1000 Monte Carlo simulations. Standardized regression coefficient (SRC) values were then calculated for the model output, which was considered as the average concentration of all organic acids inside the membrane. Based on the values and constraints for the selected parameters (Table 3) and the choice of model output, it was found that the parameters e_pores, X_d and r_p have the highest sensitivity with mostly positive correlation (Fig. 6). This is also consistent with the fact that higher membrane pore radius and higher dielectric constant (less gradient with bulk dielectric constant, which is 80 at standard conditions) results in less rejection and thus higher concentration inside the membrane. X_d, used in electroneutrality conditions inside the membrane, mostly has a positive correlation with the concentrations inside the membrane. Following these results, further model calibration was pursued by estimating only these three parameters i.e. e_pores, X_d and r_p.

3.3.2. Parameter estimation

The most sensitive parameters identified in the sensitivity analysis (e_pores, X_d and r_p) were estimated using simplex algorithm (fminsearch, MATLAB R2020b). Normalized Root Mean Square Error (NRMSE) was used as the cost function to minimize the difference between predicted and measured concentration of all organic ions in the permeate. Table 4 summarizes the estimated parameters for all the membranes. The r_p was estimated to be 0.58 ± 0.03 nm, which is rather similar across the membranes (Table 4) but higher than the values (0.41 to 0.46 nm) reported by Bargeman et al. [43] for these membranes. Nonetheless, higher values, e.g. 0.84 nm for NF270, was also reported [46].

No clear correlation was found between estimated e_pores and r_p and the feed concentration. However, there was a direct linear correlation between X_d and the feed concentration of organic acids (Table 4). Such a correlation may indicate heterogeneous ion adsorption on the membrane walls, which can be described by the Freundlich isotherm [47]. Dependency of X_d on the feed concentration was also described using an empirical equation resembling the Langmuir isotherm [34].

The best set of fitting values for e_pores, X_d and r_p reported in Table 4 are not, however, unique. These parameters are highly correlated and other combinations can result in similar good predictions. Fig. 7 is an example of a Monte Carlo simulation performed for NF270 with 10 g-SA L⁻¹ for

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### Table 3

Parameter values used for sensitivity analysis.

| Parameter   | Description                                      | Value   | Min  | Max  |
|-------------|--------------------------------------------------|---------|------|------|
| X_d (mol m⁻³) | membrane volumetric charge density               | -       | -50  | 50   |
| r_pores (-) | membrane pore dielectric constant                | -       | 30   | 80   |
| r_p (nm)   | membrane pore radius                             | -       | 0.45 | 0.8  |
| J_o (m² m⁻² s⁻¹) | permeate volumetric flux          | measured| -20% | +20% |
| ΔX (m)     | active membrane thickness                       | 2.6-6(1)| -20% | +20% |
| DS2 (m⁵ s⁻¹) | succinate diffusion coefficient                  | 9.90e-10| -20% | +20% |
| r_S2 (m)   | succinate ion Stokes radius                      | 2.52e-10| -20% | +20% |
| DA (m² s⁻¹) | acetate diffusion coefficient                    | 1.38e-9(2)| -20% | +20% |
| r_A (m)    | acetate ion Stokes radius                        | 1.94e-10| -20% | +20% |
| DF (m² s⁻¹) | formate diffusion coefficient                    | 1.84e-9(2)| -20% | +20% |
| r_F (m)    | formate ion Stokes radius                        | 2.00e-10| -20% | +20% |
| DP (m² s⁻¹) | pyruvate diffusion coefficient                   | 1.31e-9(5)| -20% | +20% |

(1) [43]; (2) [44]; (3) [21]; (4) [45]; (5) Due to lack of data, the value was assumed to be similar to lactate; (6) Calculated based on Stokes-Einstein Equation (assuming similar to lactate).
which the variability of the parameters on the prediction accuracy was evaluated through a series of 1600 simulations. Evidently, there are ranges of parameters that result in the same good predictions (Fig. 7). A similar investigation was performed by Micari et al. [36], where higher variation was also observed for $X_d$ at lower $\varepsilon_{pore}$. However, the findings of Micari et al. [36] do not show such a high variation for $X_d$ as it is shown in this study.

### 3.3.3. Model predictions

After setting the model parameters (Table 4), the simulations were performed for each experiment. Fig. 8 illustrates the rejection of all the organic compounds in three different membranes and three different synthetic broths. The diagonal line indicates a 1:1 relation between measured and predicted rejection. The model prediction was rather good for succinate in all membranes (with a 2.1% deviation on average). For the other organic ions, the deviation from the experimental data was higher partly due to measured rejections closer to zero. Acetate was underestimated and formate was overestimated in all membranes, while pyruvate was overestimated only for DL (Fig. 8).

The contributions of the different transport mechanisms of the organic ions are listed in Table 5. The driving forces are presented in percentages and are grouped in three categories: inside the membrane; feed-membrane interface; permeate-membrane interface. While the contributions of each mechanism inside the membrane (eq. (5)) is calculated based on absolute numbers, at the membrane interfaces (eq. (6) and (7)) these contributions are calculated based on log transformations (Table S4). The actual rate values are reported in Table S3. It is noteworthy that all the transport mechanisms are positive. Inside the membrane, it is apparent that diffusion has the highest contribution to the overall transport. This is mainly indicated by concentration difference across the membrane, especially for succinate and pyruvate. In absolute terms, the highest convection and electro migration is found for formate, with the highest average concentration across the membrane (Table S3). The negative rejection of pyruvate, formate, and acetate are due to dielectric exclusion. In mixed solutions containing mono and divalent ions, the divalent ions (i.e. succinate) are strongly repulsed and

![Sensitivity analysis of the selected parameters of the DSPM-DE model applied for experiments with synthetic broths. The analysis was done using standardized regression coefficient ($\beta$).](image)

**Table 4**

Estimated parameters of the DSPM-DE model, pore dielectric constant ($\varepsilon_{pore}$), volumetric charge density ($X_d$) and average membrane pore radius ($r_p$) using the simplex method, for the synthetic broths.

| Membrane | Feed concentration | $\varepsilon_{pore}$ | $X_d$(mol L$^{-1}$) | $r_p$(nm) |
|----------|--------------------|----------------------|---------------------|-----------|
| NF 270   | 10 g-SA L$^{-1}$   | 37.09                | 9.61                | 0.59      |
|          | 5 g-SA L$^{-1}$    | 38.60                | 4.88                | 0.55      |
|          | 3 g-SA L$^{-1}$    | 42.24                | 3.37                | 0.64      |
| DL       | 10 g-SA L$^{-1}$   | 36.63                | 12.45               | 0.57      |
|          | 5 g-SA L$^{-1}$    | 40.11                | 6.21                | 0.58      |
|          | 3 g-SA L$^{-1}$    | 39.00                | 3.65                | 0.58      |
| DK       | 10 g-SA L$^{-1}$   | 35.73                | 10.01               | 0.56      |
|          | 5 g-SA L$^{-1}$    | 39.04                | 4.88                | 0.59      |
|          | 3 g-SA L$^{-1}$    | 35.41                | 3.23                | 0.61      |
tend to stay further from the negatively charged membrane surface than the monovalent ions. The monovalent ions are then attracted to the membrane surface due to the Donnan effect, which consequently leads to a greater increase in the concentration of monovalent ions inside the membrane compared to in the bulk of the solution. As a result, a higher fraction of monovalent anions in a mixed salt solution than in a single salt solution will pass the membrane [12].

At the membrane interfaces, dielectric exclusion was the main rejection mechanism for all ions except pyruvate, for which the higher ion radius prevents the ion from passing through the membrane pores easily compared to other ions with smaller radius. In absolute terms, divalent succinate ion has the lowest dielectric exclusion term and the highest activity coefficient ratio. These two phenomena already cause the concentration of succinate to drop significantly (approximately 99%) at the feed-membrane interface. However, at the permeate-membrane interface the concentration increases again, on average more than six times. Study of these mechanisms reveals that most succinate rejection in fact occurs at the membrane interface and is not due to the resistance within the membrane. Such independence of selectivity on effective membrane thicknesses was also recognized by Wang and Lin [19], which confirms that rejection of solutes is determined by partitioning at the membrane surface.

Following DSPM-DE model calibration, the model was used to predict permeate concentrations of five organic ions, i.e. succinate, acetate, formate, propionate and butyrate in real fermentation broth using NF270 and DK membranes. $X_d$, $\epsilon_{\text{pore}}$ and $r_p$ values were adjusted based on the previous estimation from the most comparable synthetic broth experiment with 5 g-SA L$^{-1}$ for each corresponding membrane. Fig. 9 illustrates model predictions within the membrane and at the membrane interfaces, i.e. on the feed-membrane interface and on the permeate-membrane interface. Model uncertainty was also included by incorporating variability of $X_d$ and $\epsilon_{\text{pore}}$ obtained during parameter estimation (resulting in maximum 70% deviation from the best fit). While the model could capture the measurements for succinate and formate in the permeate, the predictions for the permeate concentration of the other organic ions were overestimated. Furthermore, as was the case for synthetic broths, most rejections occurred at the membrane interface. This phenomenon is visibly substantial in the simulation for succinate. Nevertheless, better estimation of the sensitive parameters, $X_d$ and $\epsilon_{\text{pore}}$, can perhaps improve model performance. It is noteworthy that the interference of other minor ions (not measured) as well as inorganic ions which were not considered here (only Na$^+$ was included) can also weaken the predictability potential of the model.

4. Future studies

Further experimental investigations are needed for more detailed understanding of the membrane characteristics, fermentation broth composition and operating conditions that can potentially be associated with NF separation performance with SA. Future experiments should include diafiltration and different TMPs and permeate fluxes with synthetic broths of different complexity. Dedicated experiments would enable better parameter estimation through measuring membrane $r_p$ and $X_d$ [48]. Moreover, DSPM-DE can be used to investigate the performance of the NF membranes under various conditions through scenario analysis. Concentration polarization, which was neglected in this
Conclusions

The aim of this study was to assess the performance of selected commercial NF membranes in synthetic and real SA fermentation broths. This was done through a series of experiments and modeling.

The screening revealed only marginal differences between NF270, TS40, DL and DK in rejecting SA. The SA rejection in dead-end filtration was found to be 5.3 to 170 times higher for a SA solution of 0.043 M compared with one at 0.43 M. The highest absolute SA rejection and was found to be from 5.3 to 170 times higher for a SA solution of 0.043 M.

model prediction and understanding of transport mechanisms.

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interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.seppur.2022.119904.

Fig. 9. Calibrated DSPM-DE Model used to predict the transport of organic ions for real fermentation broth for NF270 and DK membranes.
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