Dissertation

Lactic Acid Recovery from Grass Silage: Optimising the Downstream Processing Through Micro and Nanofiltration Membrane Technologies.

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A thesis for the degree of
Doctor technicae

In the
Doctoral programme in Engineering Sciences – Chemical and Process Engineering

At the
Faculty of Mechanical and Industrial Engineering,
Technische Universität Wien

Under the supervision of
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This work has received funding from the European Union's Horizon 2020 Research and Innovation Programme under the Marie Sklodowska-Curie grant agreement no. 860477 (AgRefine).

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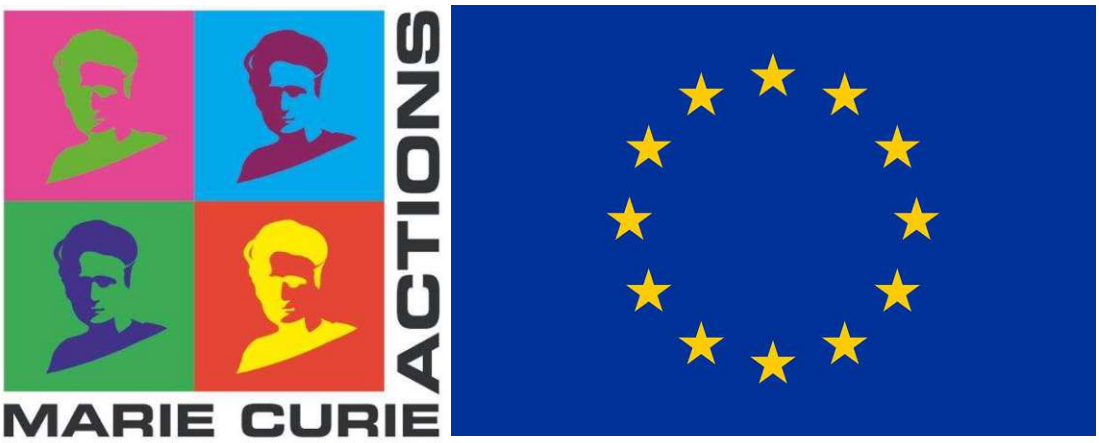

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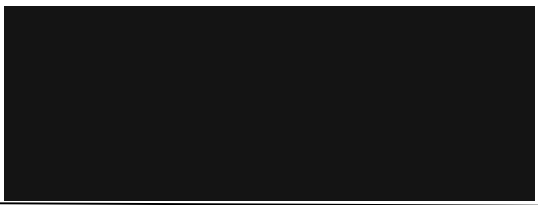

Mayuki Maryoret Vivian Cabrera González

Acknowledgements

I would like to start by giving my complete gratitude to my husband, Juan Pablo and my son, Iñigo, for their comprehensive support and trust in me to complete my dream. Without their support, this journey would not have been possible.

I would like to sincerely thank my supervisor, Ao. Univ. Prof. Dipl.-Ing. Dr. Techn. Michael Harasek, thanks for allowing me to be part of his excellent research group and integrating me into the AgRefine project. His scientific support and guidance (especially during COVID-19) have been invaluable in my professional career and have contributed to my professional growth.

A special thank and sincere gratitude to Dr Amal Ahmed for our countless hours in the lab, life conversations, scientific input, brainstorming ideas, and her support.

I would also like to express my gratitude to Dr Christian Jordan. His technical and scientific insights were precise, and his guidance was helpful and supportive during my PhD.

In addition, I would like to express my gratitude to all my colleagues on the third floor of the BI building at TU Wien and the FemChem C&I group at Getreidemarkt. All of you were very supportive in different ways, especially my friends Fernando, Camila, Barbara and Laura, for their scientific input and support during the difficult times.

Moreover, I would like to thank Dr Joseph Sweeney and all my UCD colleagues for their fantastic support during my first secondment.

Furthermore, I would like to thank Dr Marcella Fernandez de Souza for her excellent scientific support and incredible way of doing science. Also, Prof. Erik Meers, thank you for hosting me during my second secondment and, of course, all of my Ghent University colleagues.

Still, I would like to express my gratitude to the fantastic project group AgRefine; this journey would not have been possible without all of you. Thank you, ESRs: Roderick, Anna, Alexandra, Francesco, Priya, Charlene, Xavier, Srija, Rushab, Jan, Mariana, Francesca, and especially Eri and Fer!

Finally, I would like to thank the European Union, particularly the program Horizon 2020, for allowing me to complete my most wanted dream of becoming a PhD.

Kurzfassung

Diese Forschungsarbeit, die Teil des AgRefine-Projekts ist, zielt darauf ab, die Weiterverarbeitung von Milchsäure aus Grassilage und anderen Rohstoffen mit Hilfe von Membrantechnologien zu optimieren, wobei der Schwerpunkt auf der Mikrofiltration, der Nanofiltration und der Elektrodialyse im Trennungsprozess im Rahmen einer Bioraffinerie liegt. Die optimalen Bedingungen für das Downstream-Processing wurden im Labormaßstab untersucht. Die untersuchten Parameter waren der Membrantyp, die Temperatur, der Druck und der pH-Wert, um die Gewinnung und Reinheit der Milchsäure zu verbessern (***Publikation #1***). Diese Studie untersucht die Herstellung und Reinigung von Milchsäure, einer wichtigen Verbindung für die Pharma-, Lebensmittel- und Kunststoffindustrie. Durch die Bewertung von vier Nanofiltrationsmembranen (NF270, MPF-36, Toray NF, Alfa Laval NF) zielt die Forschung darauf ab, die Milchsäureausbeute durch fortschrittliche Membrantechnologie zu optimieren. Experimente, die unter verschiedenen pH- und Temperaturbedingungen durchgeführt wurden, ergaben, dass die NF270-Membran mit 71 % die höchste LA-Rückweisung lieferte, während die MPF-36-Membran mit 7 % die niedrigste Ausbeute aufwies, wenn der pH-Wert der Lösung niedriger war als der pKa-Wert der LA.

Darüber hinaus enthält ***Publikation #3*** die Behandlung eines neuartigen Ausgangsmaterials, nämlich fermentierter Süßwarenabfälle mit Gärrückständen, unter Verwendung von Milchsäurebakterien, um die Milchsäureproduktion zu steigern und sie unter optimierten Bedingungen hinsichtlich pH-Wert und Temperatur zu reinigen. Eine Konfiguration von elektrogetriebenen (Elektrodialyse und bipolare Elektrodialyse) und druckgetriebenen Membranen (Mikrofiltration und Nanofiltration) führte zu einem geringeren Energieverbrauch und einer hochkonzentrierten Milchsäurelösung aus dem innovativen fermentierten Ersatzrohstoff durch die vorgeschlagene optimierte nachgeschaltete Verarbeitung.

Bei der nachgeschalteten Verarbeitung fallen Retentate an, die reich an Verbindungen wie Zucker, organischen Säuren, Phosphat, Stickstoff und Mineralien sind. Im Rahmen dieser Optimierung wird vorgeschlagen, Retentate als Nährboden für *Chlorella vulgaris* zu behandeln (*S.* ***Publikation #4***). Dieser Ansatz zielt darauf ab, die Entstehung neuer Abfälle zu verhindern, die Produktion von Biomasse zu fördern und dem Abwasserstrom einen Mehrwert zu verleihen. Die integrierte Methode zeigt das Potenzial für eine nachhaltige Ressourcennutzung auf und unterstreicht die Bedeutung innovativer Strategien in Bioraffinerieprozessen. Darüber hinaus zeigt die erfolgreiche Kultivierung von Mikroalgen in weniger verunreinigten Strömen, wie z. B. Nanofiltrationspermeaten, neue Einblicke in Bio-Reinigungsmethoden. Insbesondere enthalten diese Ströme hohe Konzentrationen an Milchsäure und niedrige Konzentrationen an Essigsäure, so dass *Chlorella vulgaris* Essigsäure als Kohlenstoffquelle nutzen könnte. Darüber hinaus wurde das Verfahren zur Überwachung und Quantifizierung der Analyten im Grassilagesaft während der nachgeschalteten Verarbeitung sorgfältig geprüft. Standardmethoden wie Hochleistungsflüssigkeitschromatographie und Ionenchromatographie sowie neuartige Techniken wie Ganzzell-Biosensoren wurden auf ihre Wirksamkeit bei der Überwachung der Analyten getestet.

Schließlich wurde eine Diskussion über die im AgRefine-Projekt entwickelten Bioraffinerie-Technologien als vereinfachtes Modell (Publikation #2) vorgeschlagen, das unter extremen Bedingungen, einschließlich der Atacama- und Sonoran-Wüste, angewendet werden kann, um ihre breite Anwendbarkeit und ihren potenziellen Nutzen zu demonstrieren.

Abstract

This research, part of the AgRefine project, aims to optimise the downstream processing of lactic acid derived from grass silage and other feedstocks using membrane technologies with a focus on microfiltration, nanofiltration and electrodialysis in the separation process within a biorefinery context. The optimal conditions for the downstream processing were investigated at a laboratory scale. The considered evaluated parameters were membrane type, temperature, pressure, and pH to enhance the recovery and purity of lactic acid (***Publication #1***). This study investigates the production and purification of lactic acid, a crucial compound for the pharmaceutical, food, and plastic industries. By evaluating four nanofiltration membranes (NF270, MPF-36, Toray NF, Alfa Laval NF), the research aims to optimise lactic acid yield through advanced membrane technology. Experiments conducted under varying pH and temperature conditions revealed that the NF270 membrane provided the highest LA rejection at 71%, whereas the MPF-36 membrane showed the lowest at 7% when the pH of the solution was lower than the LA pKa.

Additionally, ***Publication #3*** includes the treatment of novel feedstock, fermented candy waste with digestate, using lactic acid bacteria to increase the production of lactic acid and purify it under optimised conditions regarding pH and temperature. A configuration of electro-driven (electrodialysis and bipolar electrodialysis) and pressure-driven membranes (microfiltration and nanofiltration) resulted in lower energy consumption and a high-concentrated solution of lactic acid from the innovative fermented substitute feedstock by the proposed optimised downstream processing.

During the downstream processing, retentates are generated, which are rich in compounds like sugars, organic acids, phosphate, nitrogen and

minerals. As part of this optimisation, it is proposed that retentates could be treated as a culture medium for *Chlorella vulgaris (S.* ***Publication #4****)*. This approach aims to prevent new waste generation, promote biomass production, and add value to the effluent stream. The integrated method showcases the potential for sustainable resource utilisation and highlights the importance of innovative strategies in biorefinery processes. Moreover, the successful cultivation of microalgae in less contaminated streams, such as nanofiltration permeates, demonstrates new insights into bio-purification methods. Specifically, these streams contain high concentrations of lactic acid and low concentrations of acetic acid, which *Chlorella vulgaris* could use acetic acid as a carbon source. Moreover, the process of monitoring and quantifying the analytes in the grass silage juice during downstream processing was carefully considered. Standard methods like high-performance liquid chromatography and ion chromatography, as well as novel techniques like whole-cell biosensors, were tested for their effectiveness in monitoring the analytes.

Finally, a discussion about the biorefinery technologies developed in the AgRefine project were suggested as a simplified model (***Publication #2***) to be applied in extreme conditions environments, including the Atacama and Sonoran deserts, demonstrating their broad applicability and potential benefits.

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List of Abbreviations

ANOVA	Analysis of Variance
BOKU	Universität für Bodenkultur
BPED	Bipolar Electrodialysis
CEM	Cation Exchange Membranes
DM	Dry Matter
DOI	Digital Object Identifier
ED	Electrodialysis
ENP	Extended Nernst-Planck Equation
ESRs	Early Stage Researchers
EU	European Union
EUBCE	European Biomass Conference & Exhibition
GJ	Green Juice
GSJ	Grass Silage Juice
HPLC	High-Performance Liquid Chromatography
ISBN	International Standard Book Number
ITN	International Training Network
LA	Lactic Acid
LAB	Lactic Acid Bacteria
LCD	Limiting Current Density
MBR	Membrane Bioreactor
MED	Monopolar Electrodialysis
MF	Microfiltration
MFP	Microfiltration Permeate
MFR	Microfiltration Retentate
MWCO	Molecular Weight Cut-Off
NF	Nanofiltration
NFP	Nanofiltration Permeate
NFR	Nanofiltration Retentate
P	Permeate
ppm	Part per million
PV	Process Validation
R	Retentate
SA	Succinic Acid
SDEWES	Conference on Sustainable Development of Energy, Water and Environment Systems

SL	Synthetic Leachates
TCA	Tricarboxylic Acid Cycle
TKN	Total Kjeldahl Nitrogen
TPB	Three Phases Bioreactor
TS	Total Solids
TU Wien	Technische Universität Wien
UCD	University College Dublin
UF	Ultrafiltration
UV	Ultraviolet
VS	Volatile Solids
WUR	Wageningen University & Research

List of appended publications

I. Journal Publications

Journal Publication #1	**Mayuki Cabrera-González,** Amal Ahmed, Khaled Maamo, Mohammad Salem, Christian Jordan, Michael Harasek. **Evaluation of Nanofiltration Membranes for Pure Lactic Acid Permeability** **Membranes 2022, 12(3), 302.** **https://doi.org/10.3390/membranes12030302**
Journal Publication #2	**Mayuki Cabrera-González,** Fernando Ramonet, Michael Harasek. **Development of a Model for the Implementation of the Circular Economy in Desert Coastal Regions** **Land 2022, 11(9), 1506.** **https://doi.org/10.3390/land11091506**
Journal Publication #3	**Eleftheria Papadopoulou**, **Mayuki Cabrera-González,** Daniela Reif, Amal Ahmed, Panagiotis Tsapekos, Irini Angelidaki, Michael Harasek. **Separation of Lactic Acid from Fermented Residual Resources using Membrane Technology.** **Journal of Environmental Chemical Engineering, 2023, 11(5), 110881.** **https://doi.org/10.1016/j.jece.2023.110881**
Journal Publication #4 (Submitted)	**Mayuki Cabrera-González**, Marcella Fernandes de Souza, Erik Meers, Amal Ahmed, Michael Harasek. **Production of *Chlorella vulgaris* using grass silage juice and secondary effluents from lactic acid recovery through pressure-driven membranes** Journal of Algal Research

II. Co-Author publications

Journal Publication #5 (Submitted)	Charlene Vance, Maneesh Kumar Mediboyina, Eleftheria Papadopoulou, **Mayuki Cabrera-González**, Daniela Reif, Joseph Sweeney, Michael Harasek, Fionnuala Murphy. **Using process modelling and optimisation to determine the sustainability of a novel lactic acid biorefinery in Europe: Influence of process improvements, scale, energy source, and market conditions** **Journal of Cleaner Production**

III. Public Reports

Public Report #1	**Mayuki Cabrera-González,** Alexandra Nastouli, Eleftheria Papadopoulou, Priya Pollard, Roderick van Roosmalen, Francesco Vigato, Anna Visentin. **Deliverable 1.1 State of the Art Report on Anaerobic Digestion and Biorefinery Technologies.** **Ref. Ares (2021)2242526 - 31/03/2021**
Public Report #2	**Mayuki Cabrera-González** **Deliverable 1.8 Downstream Processing Strategy + Process Simulation Model** **Ref. Ares (Submitted) 2022.**
Public Report #3	**Mayuki Cabrera-González,** Srija Balachandran. **Deliverable 1.9 Technology Integration and Product Separation Optimisation** **Ref. Ares (Submitted) 2024.**
Public Report #4	**Mayuki Cabrera-González,** Eleftheria Papadopoulou, Priya Pollard, Francesco Vigato. **Deliverable 1.10 Assessment of TPB-3rd Phase Adaptation to Alternative Input.** **Ref. Ares (Submitted) 2023.**

IV. Conference Publications

Conference Poster #1	**Mayuki Cabrera-González,** Fernando Ramonet, Michael Harasek. **Development of a Model for the Implementation of the Circular Economy in Desert Coastal Regions** **Circular@WUR: Living within planetary boundaries, Wageningen University and Research, Wageningen, 11th-13th April 2022. DOI: 10.13140/RG.2.2.21658.11200**
Conference Poster #2	**Mayuki Cabrera-González,** Amal Ahmed, Khaled Maamo, Mohammad Salem, Christian Jordan, Michael Harasek. **Effect of the Influence of Glucose and Fructose on Lactic Acid Recovery. 30th European Biomass Conference & Exhibition (EUBCE2022). Paris, France (Online), 9th -12th May 2022.**
Conference Poster #3	**Mayuki Cabrera-González,** Amal Ahmed, Khaled Maamo, Mohammad Salem, Christian Jordan, Michael Harasek. **Evaluation of Nanofiltration Membranes for Pure Lactic Acid Permeability** **Biorefine Conference 'The role of biorefineries in European agriculture'. Ghent, Belgium, 30th-31st May, 2022**
Conference Proceedings #4	**Mayuki Cabrera-González,** Amal Ahmed, Michael Harasek. **Isolation and downstream processing of high-value products from preserved brown seaweed – A Literature Review.** **7th Minisymposium Verfahrenstechnik and 8th Partikelforum, BOKU, Vienna, April 13th – 14th, 2023, ISBN: 978-3-900397-08-1**
Oral Presentation 1	**Mayuki Cabrera-González,** Marcella Fernandes De Souza, Erik Meers, Amal Ahmed, Michael Harasek. **Production of Microalgae Biomass Using Grass Silage Juice and Side Streams from the Downstream Processing of Lactic Acid.** **SDEWES 2023-0419**

V. Master Theses Guidance

Thesis #1	**Khaled Maamo** **Influence of the Sugars Present in Grass Silage Model Solution on Lactic Acid Recovery Through Nanofiltration Process.** **18/01/2022** **DOI: 10.34726/hss.2022.92284**
Thesis #2	**Mohammad Salem** **Investigation of the Presence of Minerals on the Lactic Acid Recovery Using Membrane Technology.** **18/01/2022** **DOI: 10.34726/hss.2022.92285**
Thesis #3	**Timo Niklas Widmann** **Separation of Lactic Acid from Grass Silage by Multistage Membrane Processes.** **24/04/2024** **DOI: 10.34726/hss.2024.115405**

Chapter 1:Introduction.

In 2015, the United Nations published an international set of 17 Sustainable Development Goals (Figure 1), settling the importance of sustainable development across various sectors. Mainly, among the 17 goals, goal two emphasises sustainable agriculture. By 2030, it guarantees the establishment of a sustainable food production system and the adoption of resilient agricultural practices. Meanwhile, goal number 12, targeted for achievement by 2020, focuses on responsible handling of chemicals and waste at every stage of their life cycle. It means decreasing the releasement into the water bodies, atmosphere, and soil to mitigate their adverse effects on human health and the environment. In addition, this goal promotes the prevention of substantially reduced waste generation through recycling and reuse, employing a sustainable approach (United Nations, 2015).

Figure 1. Sustainable Development Goals

The most promising avenue for addressing the challenge of sustainable agricultural development rests in the continual innovation process using, for example, modern genetic and information technologies (Basso & Antle, 2020).

This approach aims to improve agricultural productivity while harmonising economic, environmental, and social outcomes inherent in agriculture and the food system (Basso & Antle, 2020).

Furthermore, the European Commission has demonstrated that it is fully committed to transforming the EU into a resource-efficient, competitive, and clean economy under the aims of the Paris Agreement (European Commission, 2024). To make Europe the first climate-neutral continent of the earth, the EU designed the European Green Deal to ensure zero emissions by 2050 and in 2021, the EU implemented its first European Climate Law, with a goal of 55% less emissions by 2030 and an additional target in February 2024 up to 90% reduced emissions by 2040 (European Commission, 2024). Moreover, a sustainable future that meets the European Green Deal can be helped by a circular economy supported by the different EU initiatives like the Biodiversity Strategy, the Farm to Fork Strategy and the Circular Economy Action Plan (Platt et al., 2021). An essential factor for a circular economy or circular bio-based economy and the EU's transition to a climate-neutral economy is biorefineries, focusing on the one which manufactures bio-based chemicals and materials (Platt et al., 2021).

A biorefinery is a system or facility designed to efficiently utilise biomass to generate various products while trying to be self-sustaining and environmentally friendly (Saral et al., 2021). Biorefineries present a green, sustainable approach by utilising waste as a potential feedstock, transforming an undervalued stream into a valuable resource. This strategy aims to generate a range of marketable products on a significant scale (Awasthi et al., 2022). The European Union, in the past couple of decades, has been gradually promoting research in biorefinery as one of the essential components of the bioeconomy. Thus, it has funded a variety of projects concerning biorefineries. One of the projects that the EU has funded under Horizon 2020 has been BIOFOREVER

(**BIO**-based products from **FOR**estry via **E**conomically **V**iable **E**uropean **R**outes), which focused on the lignocellulosic biorefinery and markets (Grant Agreement 720710, 2018). Another HORIZON 2020 project is currently being executed under the name CIRCULAR BIOCARBON (Turning carbon of complex organic urban waste streams into value-added products), which focuses on the valorisation of organic fraction of municipal solid waste through the biorefinery concept (Grant Agreement 101023280, 2021). Besides the mentioned projects, HORIZON 2020 has also focused on the professional formation of bioeconomy leaders with a focus on the agricultural industry over biorefineries; in this case, it has funded the project AgRefine, which is an International Training Network programme (ITN) in which the author participated.

The project AgRefine specialises in developing and applying innovative technologies and systems, including biosensors for monitoring and control, biorefinery process, purification methods for removing contaminants from grass silage or other feedstock through downstream processing (i.e. lactic acid purification), and the production of high-value compounds like bio-succinic acid (SA). This goal is proposed by employing an integrated cascade approach that consistently achieves each substrate input's most valuable valorisation pathway. Therefore, this research aims to design a procedural pathway and adaptable downstream processing technology for separating and recovering lactic acid, guaranteeing the creation of marketable product streams.

Finally, the EU is actively pursuing increased resource efficiency and transitioning towards a bio-based economy. This aims to achieve sustainable production of renewable resources and establish a mechanism to maximise the production of food, feed, bio-based products, biofuels, and bioenergy (Grant Agreement 860477, 2019) with the effort on the emphasis on training highly qualified personnel to pursue these goals effectively.

1.1 Objectives

The objectives of this research were defined explicitly by the AgRefine project to this thesis's author. The main aims are:

- Application of membrane technologies to optimise lactic acid downstream processes from model solutions and grass silage.
- Determination of the exact composition, including concentration and compounds, of grass silage leachates produced during the first phase of silage-press liquor and downstream processing. This will be achieved using standard qualitative and quantitative chemistry methods, such as High-Performance Liquid Chromatography (HPLC) or Ion Chromatography, along with the novel technology of biosensors for enhanced detection and analysis.
- Implementation of the optimised downstream processing techniques for lactic acid recovery from a fermented substitute feedstock.

In addition to the defined objectives of the project, sub-objectives were defined by the author of this thesis:

1.1.1 Sub-objective

The following sub-objectives were pursued to purify and concentrate lactic acid from grass silage and fermented substitute feedstock using membrane technologies:

- Identification of the optimal micro or nanofiltration membranes for lactic acid recovery.
- Determination of the operation conditions for downstream processing using membrane technologies as a separation process.
- Implementation of an integrated biorefinery system with synergistic benefits by cultivating microalgae as a possible way to achieve a zero-liquid discharge approach.

1.2 Research Questions

The main task was using membrane technologies to purify lactic acid, focusing on micro and nanofiltration from grass silage. The following questions were asked to carry out the objectives.

1) What are the optimal operating conditions for the micro and nanofiltration to obtain higher lactic acid concentrations using grass silage juice as a feedstock?
2) Is the designed downstream processing applicable for an alternative substrate?
3) What strategies can be applicable to minimise the waste generation after the downstream processing of lactic acid?

1.3 Thesis Structure

This thesis is focused on developing downstream processing using micro and nanofiltration membranes to recover lactic acid from grass silage and other fermented products (Figure 2). The results of the thesis and research are presented and published in scientific journals (peer-reviewed), conferences, and public reports.

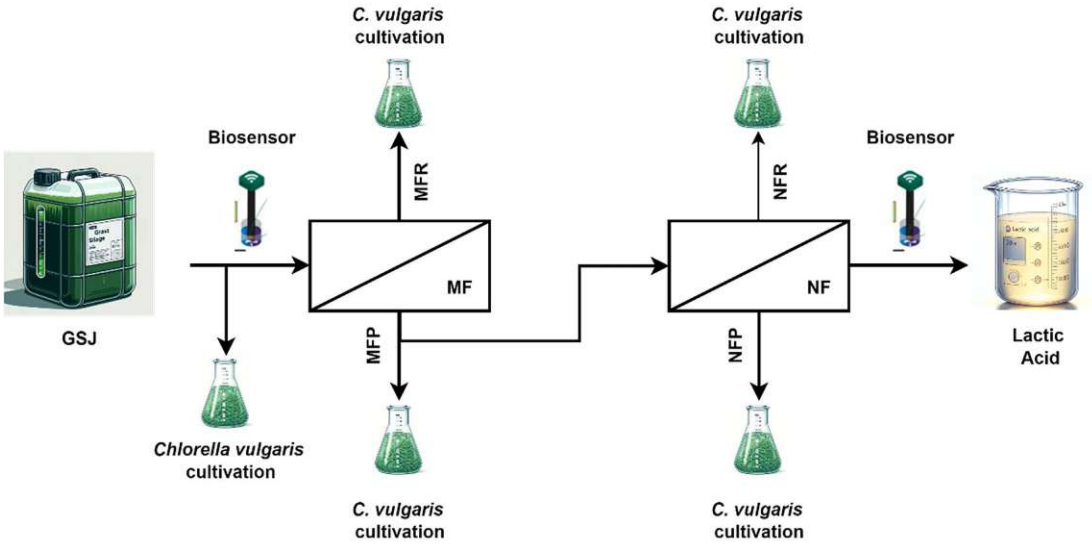

Figure 2. Graphical Abstract. GSJ: Grass Silage Juice, MF: Microfiltration, NF: Nanofiltration, MFR: Microfiltration Retentate, MFP: Microfiltration Permeate, NFP: Nanofiltration Permeate, and NFR: Nanofiltration Retentate.

This thesis will be structured as follows:

Chapter 1. Introduction, where the main motivation, objectives, and research question of the AgRefine project are presented.

Chapter 2. Application of Pressure-Driven Membranes Technologies in Green Biorefineries, where a literature review is presented about the technology applied.

Chapter 3. *Chlorella vulgaris* Cultivation Utilising Effluent Streams from Lactic Acid Downstream Processing of Grass Silage Juice, where an innovative process is presented to produce microalgal biomass.

Chapter 4. Process Validation of the Downstream Processing of Lactic Acid Using a Substitute Fermented Feedstock, where a fermented high sugar

content feedstock (candy waste and digestate) was purified using membrane technologies.

Chapter 5. Analytics – Biosensor where an inline technology is presented to measure certain compounds in real-time.

Chapter 6. Perspective of a simplified model for circular economy in extreme environmental conditions, where the technologies developed in this thesis are suggested to be applied in environments with extreme conditions like the Atacama and Sonora deserts in Chile and Mexico, respectively.

Chapter 7. Conclusions

Chapter 8. Scientific articles where the author presents ***Publication #1, #2, #3, and #4***.

Chapter 2: Application of Pressure-Driven Membranes Technologies in Green Biorefineries.

Sustainable biomasses, such as green biomasses, are promising and versatile feedstock that can be used for animal feeding and obtaining proteins and bio-based products for food, cosmetics, pharmaceutical and chemical industries (Gaffey et al., 2023). Green biomass, which includes green crops like carrot leaves, legumes such as clover and alfalfa, and grasses, is considered a sustainable option for biorefineries. The advantages of using green feedstock are that it is low-priced and can be produced in large quantities. For example, in Europe, one-third of the agricultural area belongs to grassland (Kamm et al., 2016), and this grass may be converted into new compounds to prevent and reduce farm waste effectively.

Green crops can be fresh or ensiled as feed in green biorefinery (Lübeck & Lübeck, 2019). Ensiling, one of the primary methods for treating and preserving green biomass, is a common agricultural practice that helps to avoid the shortage of grass during seasons like autumn and winter. The ensiling process involves harvesting the grass, chopping it into small pieces, and then pressing and fermenting it under anaerobic conditions. After fermentation, the grass fractionation products can be converted into several organic compounds (Badgujar & Bhanage, 2018).

Once the grass is pressed, it fractionates into a solid and a liquid fraction. The liquid fraction is known as green juice. Green juice (GJ) is a rich source of organic acids, sugars, amino acids and minerals. Within the sugar's compounds, glucose and fructose are the main sugars contained in GJ. On the other hand, organic acids contained in GJ are lactic acid (LA), butyric acid, formic acid, and acetic acid, LA being the most concentrated one. These chemical compounds can be recovered by combining various technologies like

membranes, centrifugation, distillation, adsorption, and evaporation. In addition to that, GJ can also be a feedstock for anaerobic digestion (Feng et al., 2021; Steinbrenner et al., 2022).

LA (Figure 3) is a monomer organic acid used in several industries like food preservation, pharmaceuticals, detergents, and cosmetics, making this molecule essential due to widespread applications. Its chemical formula is $CH_3CH(OH)COOH$, and its pK_a is 3.86 (Wardi et al., 2020). LA, known for its remarkable versatility, has recently gained significant attention as a key ingredient in producing poly-lactic acid (Bühlmann et al., 2022), a biodegradable bioplastic.

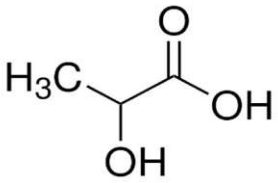

Figure 3. DL-Lactic acid. Source: Merck.

Different feedstocks have been utilised for LA production to look for the replacement of the oil-based material; this research will only contemplate green biomass. In the last decade, polymers based on LA have been a particular concern in medicine because the human body can degrade it by hydrolysis of the ester backbone to non-noxious and non-lethal compounds (Zamanova et al., 2014).

The industrial application of LA depends on its isomeric forms, and they can be as D(-) or L(+) isomers or a mixture of them. Pure LA isomers are more valuable (Dietz et al., 2016) than impure ones. Therefore, special attention is paid to producing these enantiomers. LA is generally produced in two ways: biotechnological route or chemical synthesis. Lactic Acid Bacteria (LAB) like *Lactobacillus plantarum*, *Pediococcus acidilactici*, *Enterococcus mundtii* (Mora-

Villalobos et al., 2020), and filamentous fungi like *Rhizopus oryzae* and *Aspergillus oryzae* (Melo et al., 2024) can ferment streams that contain sugars. However, several modified microorganisms, such as the yeast *Komagatataela phaffii* (Melo et al., 2020), can express LA genes supported by genetic engineering to improve LA productivity. From a practical point of view, the biological route of LA production is advantageous compared to chemical synthesis because this process is environmentally friendly and safer, and the products are optically pure (Karnaouri et al., 2020). For these reasons, the fermentation process for lactic acid production is used worldwide (Eş et al., 2018), and the production of LA worldwide is approx. 32,500 tons of lactic acid per year (Adom & Dunn, 2016), and China produced almost 80,000 tons annually in 2020 (Jem & Tan, 2020). This opportunity directly leads to integrating biorefineries and advanced technologies, which is crucial for optimising biomass usage and reducing waste generation by converting lower-value streams into raw materials for higher-value products (Allan Andrade et al., 2023). The success and contributions of biorefineries rely heavily on the availability of highly selective and energy-efficient separation technologies. These technologies are crucial for ensuring the sustainable production of chemical compounds at an industrial scale, making membrane technologies an ideal choice (Lipnizki et al., 2019).

Membrane technologies are used in the downstream processing of a target product and are also a part of the biorefinery process to obtain various marketable products. Membranes have been used to separate sugars from the liquid feedstock, like grass silage, the concentration of organic acids, and removing microorganisms and big molecules. The use of membranes is due to the advantages of being highly selective in separation processes. It means obtaining a highly pure product or chemical compound is possible, with low

energy demand, and it is easy to scale from lab to industrial scale (Yogarathinam et al., 2020).

Critical processes in biorefineries are significantly influenced by the use of pressure-driven membranes (Figure 4), which are established for each membrane type according to its pore sizes, including microfiltration, ultrafiltration, nanofiltration, and reverse osmosis. Microfiltration (MF) has the largest pore size (0.1-10 μm), operates at the lowest processing pressure (0.1-2 bar) (Carter et al., 2021) and is primarily used to remove microorganisms (10 – 100 μm), spores, and big molecules. In the industrial process, MF is the initial step for clarifying fermented broths (Gul et al., 2021; Lipnizki et al., 2019). Ultrafiltration (UF) is an advanced separation technology used in a wide range of industries. It has a pore size of 0.001 – 0.05 μm and operates between 2 to 5 bar of pressure (Singh & Hankins, 2016). This method, which originated as a fraction method in the late 1960s, has since then evolved and expanded. UF membranes have seen ongoing development and improvement, extending their application to various fields, including chemical recovery, cell harvesting, dairy processing, medical applications, wastewater reclamation, water treatment and juice concentration. Its primary applications focus on purifying and concentrating macromolecules (Al Aani et al., 2020). Nanofiltration (NF), with a molecular weight cut off between 100 – 2000 Da (Shao et al., 2022), operates between 5 to 60 bar. NF is used for various separations, including partial demineralisation, water demineralisation, textile wastewater treatment, and purification processes in the food, pharmaceutical and biotechnological industries (Bowen & Welfoot, 2002), as well as for the pre-concentration of organic acids.

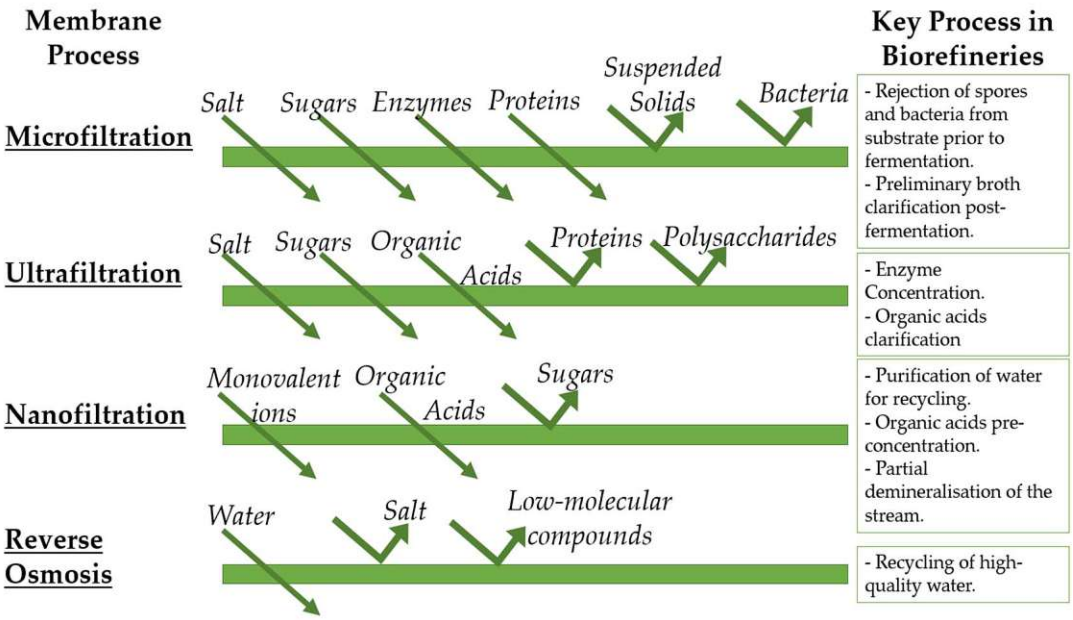

Figure 4. Pressure-driven membrane key processes in biorefineries. Based on Lipnizki et al., 2019

In the last decade, nanofiltration membrane technology has increased in importance in many industries, specifically biotechnology. The use of membranes in the separation process of LA is widely used due to several advantages. High selectivity and levels of purification, flexibility in the scale of production, and the possibility of integration with other technologies, i.e. reactors and fermenters, are the most important advantages. However, some disadvantages must be considered, such as the high cost and fouling issues (Komesu et al., 2017).

Given the complexity and expense associated with the downstream processing, a crucial purification step to recover LA from green biomass, it is clear why such advanced technologies are necessary. The cost of this phase accounts for 50% (Komesu et al., 2017) and 80% (Taleghani et al., 2018) of the total production, underlining the importance of optimising these processes for both efficiency and cost reduction (Ecker et al., 2012).

In this context, nanofiltration membranes are used in downstream processing due to their ability to separate proteins, nutrients, cells, unconverted carbon sources and salts (Pal et al. 2009) from the fermented broth. Technology integration plays a vital role in addressing the advantages and challenges of nanofiltration in the biotechnological industry.

To address the problem of efficiency and effective methods of purifying lactic acid, ***Publication #1*** (Cabrera-González et al., 2022) was published. ***Publication #1***, named "Evaluation of Nanofiltration Membranes for Pure Lactic Acid Permeability", has industrial relevance in the sense of providing initial insights on how different commercially available nanofiltration membranes can be utilised to efficiently purify lactic acid, with a focus on the operation conditions to optimise the performance at laboratory scale by using the membrane system equipment OS-MC-01 (Figure 5). In addition, by evaluating four different nanofiltration membranes (NF 270, MPF-36, Toray NF and Alfa Laval NF) by changing pH (2.8, 3.9 and 6.0) and temperature (25 °C and 40 °C) in the operation conditions shows the influence of it for the separation process, which is crucial for designing more effective separation process in industrial application. Moreover, ***Publication #1*** indicates a set of experimental data at the laboratory scale, which can be used for scaling up the nanofiltration process from lab to industrial scale, a standard gap in membrane research.

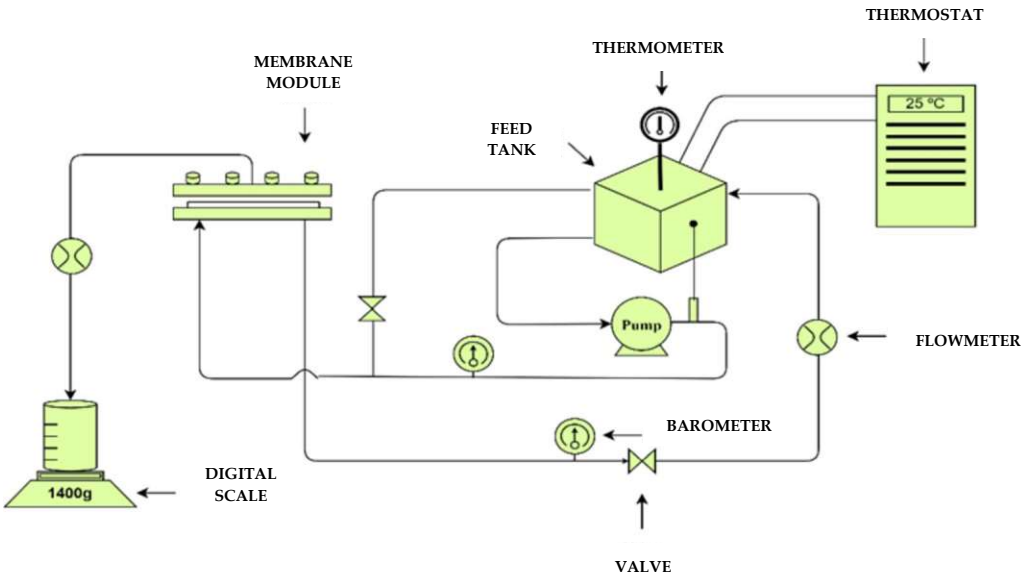

Figure 5. Membrane System Equipment (Model OS-MC-01). Adapted from Cabrera-González et al.

The evaluation of different nanofiltration membranes is related to membrane permeability. Membrane permeability is a crucial characteristic of membranes that controls the movement of solutes and solvents through them (Fralliccardi et al., 2022). The pores in the membrane can facilitate the movement or permeation through diffusion. However, established mechanisms prevent specific molecules from permeating, such as size exclusion (sieving mechanism), dielectric exclusion and Donnan exclusion (Suhalim et al., 2022). The fundamental principle of size exclusion membranes is that their pore sizes are smaller than the pollutants, and the Donnan effect describes the interaction between a charged membrane and ionic solutes (Mautner, 2020). If the membrane is negatively charged, it repels anions (negatively charged ions) and allows cations (positively charged ions) to pass through. On the contrary, if the membrane is positively charged, it repels cations and allows anions to pass (T. Zhang et al., 2023). To provide a mathematical explanation, the extended Nernst-Planck Equation (ENP)

describes the transport of solutes (Eq. 1) through the pores of the selective layer (Cevallos-Cueva et al., 2024; Szymczyk et al., 2003).

$$J_i = -K_{i,d} D_{i,\infty} \frac{dc_i}{dx} - \frac{z_i F c_i K_{i,d} D_{i,\infty}}{RT} \frac{d\psi}{dx} + K_{i,a} c_i J_v \qquad \text{Eq. 1}$$

Eq. 1 represents three different membrane phenomena: diffusion, electromigration and advection (Cevallos-Cueva et al., 2024) where $K_{i,d}$ is the hindrance factor of diffusion (-); $D_{i,\infty}$ is the diffusion coefficient of species i in the bulk ($m^2 s^{-1}$); c_i is the concentration of species i in the membrane active layer (mol m^3); x is the coordinate in the direction to the permeate side (m); z_i is the ion valence (-); F is the Faraday constant (96500 C mol^{-1}); R is the ideal gas constant (8.314 J K^{-1} mol^{-1}); T is the temperature (K); ψ is the electrical potential in the active layer (V); $K_{i,a}$ is the hindrance factor of advection (-) and J_v is the solution flux (m s^{-1}).

Regarding this theoretical framework, ***Publication #1*** focused on practical performance metrics. Precisely, two parameters were measured to estimate the performance of the membrane: permeate flux and removal efficiency. Permeate flux describes the permeate quantity produced during membrane separation per unit of time and NF membrane area (Alonso et al., 2020). The Eq. 2 characterises the permeate flux.

$$J_P = \frac{Q_o}{A} \qquad \text{Eq. 2}$$

Where J_P is the permeate flux, A is the area in m^2, Q_O is the flow (Kg h^{-1}).

The capital and operational costs of membrane systems are directly influenced by membrane permeate flux. Therefore, permeate flux is critical to designing a membrane process (Ji, 2015).

Another parameter to evaluate is the salt rejection (%). It is crucial for evaluating the performance of membrane separation processes. It belongs to the fraction of a solute that is retained by the membrane (Retentate) and does not pass into the permeate streams. Eq. 3 represents the mathematical calculation of the rejection.

$$R = \left(1 - \frac{C_p}{C_f}\right) \times 100 \qquad \text{Eq. 3}$$

R is the rejection (%), C_P is the permeate concentration (g L^{-1}), and C_f is the feed concentration (g L^{-1}).

In addition to that, two real-time parameters were measured: pH and conductivity. These parameters were studied to evaluate if the pH change would affect the membrane surface (Cabrera-González et al., 2022; Yoon et al., 2005). The effect of pH and the change in conductivity is primarily observed through changes in membrane flux, solute rejection and fouling rejection; therefore, the pH on the solution plays an essential role in having a quick overview of the separation performance, as well as the conductivity (Luo & Wan, 2013).

The optimal performance at the highest lactic acid permeability at pH 2.8 and temperature 25 °C was for the membrane MPF-36 with a permeability of 93 %, mainly attributed to the membrane's loose structure and large pore size

(MWCO 1000 Da). In addition, the lowest rejection happened for all the membranes when the pH dropped to 2.8. Due to the LA's non-dissociation at that pH, it remains neutrally charged; therefore, this consequence is associated with the Donnan exclusion effect.

A laboratory-scale setup is ideal to start up due to several reasons. It requires less time, can work in a limited space, and potentially can be cheaper. Additionally, it allows the collection of extensive data and the execution of multiple processes under changing conditions simultaneously (Dholiya et al., 2023).

Although ***Publication #1*** presents advantageous results, it can also be criticised for the lack of deep research into economic analysis, environmental impact, and the test of membranes regarding longevity and fouling. Moreover, the rejection of lactic acid by screening membranes and operating conditions can be improved by implementing another type of technology or nanofiltration step. Finally, no impurities were added to the research process, and it could result in entirely different results.

However, a novel bio-purification process using an engineered *E.coli* strain was proposed by Nastouli et al., 2024, after using flat-sheet nanofiltration membranes as a primary downstream processing. The impurities of the synthetic solution were successfully removed. Impurities, like acetic acid and glucose, were considered from a model solution of grass silage containing LA using a membrane bioreactor (MBR). Implementing bio purification could be an essential step after nanofiltration due to the high concentration of acetic acid in the nanofiltration permeate. Therefore, integrating these two processes might result in a high purity and concentration of LA.

Chapter 3: *Chlorella vulgaris* Cultivation utilising Effluent Streams from Lactic Acid Downstream Processing of Grass Silage Juice.

The potential to valorise effluent streams or secondary effluents (retentates) from membrane processes is a topic that has been recently considered. This issue represents a significant drawback of membrane separation technology, which has not been extensively addressed (Chen et al., 2021). A secondary effluent in this research will be defined as the stream containing a fraction of chemical compounds that are not utilised for further purification and, therefore, discarded. In this case, the retentates from the downstream processing by membrane technology from grass silage juice. The recovery of the by-products or the use of secondary effluents for other purposes rather than disposal could be beneficial from an environmental and economic perspective (Rezende Moreira et al., 2022).

The retentates offer significant advantages due to their retention of essential nutrients, such as phosphorus, nitrogen, sugars, minerals and organic acids, which are not further purified. These compounds are contained in a considerable concentration, making the retentates a valuable resource for potential microalgae cultivation.

Several authors pointed out that agroindustrial waste is useful for microalgae production (de Carvalho et al., 2018; Santhana Kumar et al., 2022; C. Zhang et al., 2021) due to the high content of carbon sources, nitrogen, phosphate and different minerals. The possibility of the application of secondary effluents for microbiological purposes has received little attention in the literature up to now; it means there is a gap in its analysis that can be complemented through the research done by this thesis.

Rezende Moreira et al. summarised extensive applications for treating secondary effluents using membranes. Among the hybrid separation

processes shown, mixing MF, NF or UF and ED, and so on, the most recovered by-product is water, independent of the used stream. One of the examples given by the authors was a raw leachate purification process using an aerobic membrane bioreactor, MF and NF, where the by-products recovered were N- NH_3 and water for reuse. Nevertheless, there was a NF concentrate stream that was not further processed. Properly treating retentate from membrane processes creates a bottleneck that currently limits the extensive application of membrane separation technology in waste treatment (Chen et al., 2021). In this context, the challenge highlights the need for innovative solutions to be able to utilise by-products efficiently.

Specific strategies and technologies are being implemented to explore potential uses and reduce the production of secondary effluents. All streams from the downstream processing of recovering lactic acid from grass silage juice (Table 1) were utilised as a culture medium for the production of microalgae, specifically *Chlorella vulgaris*.

The streams used were grass silage juice (GSJ), which is the initial feedstock (Figure 6), microfiltration retentate (MFR), microfiltration permeate (MFP), nanofiltration retentate (NFR) and nanofiltration permeate (NFP). All of these streams were diluted to decrease their brownish, except NFP, and allow adequate light penetration, essential for the growth of photoautotrophic microalgae.

Figure 6. *Chlorella vulgaris* cultivation, on the left in a control medium (Bolt Basal Medium), on the right in GSJ diluted 20x.

Cultivating microalgae in effluents presents significant challenges due to algae's specific requirements and nature. In a circular bioeconomy, recycling is fundamental, and the capacity of microalgae to bioremediate or convert nutrients is highly valuable (Nagarajan et al., 2020). The biomass of microalgae plays an essential role in the circular bioeconomy, where secondary effluent valorisation can be effectively achieved by using microalgae as a bioremediatory agent (Satya et al., 2023).

The research proposes using secondary effluent as a culture medium for microalgae for its characteristic advantages. Additionally, ***Publication #4*** suggests that microalgae cultivation could be an additional step in lactic acid purification for the NFP (**Submitted *Publication #4***). This is because microalgae can uptake acetic acid, which remains partially unrejected during the downstream processing, as a carbon source to support their growth (Li et al., 2022; Yu et al., 2020). This approach enhances the overall purification process.

Table 1. Grass Silage Juice Composition

pH	4.74	**Fe [ppm]**	30.622
Conductivity [mS/cm]	9.81	**Mn [ppm]**	6.63
TKN [ppm]	194.17	**Mg [ppm]**	132.20
Glucose [ppm]	5189.11	**Na [ppm]**	13.80
Fructose [ppm]	5054.49	**Ca [ppm]**	692.20
Succinic acid [ppm]	1111.64	**K [ppm]**	2576.30
Lactic acid [ppm]	5797.77	**Al [ppm]**	11.13
Acetic acid [ppm]	1262.09	**Cd [ppm]**	2.60
Pyroglutamic acid [ppm]	83.40	**Co [ppm]**	2.42
Ethanol [ppm]	164.55	**Cr [ppm]**	3.40
Propionic acid [ppm]	882.99	**Cu [ppm]**	1.64
P [ppm]	251.14	**Ni [ppm]**	2.3571
S [ppm]	40.02	**Zn [ppm]**	4.04

Overall, growing microalgae in wastewater or secondary effluents provides a source of biomass and positively impacts the food-energy-water nexus, making it a crucial component of the environment (Hasnain et al., 2023). This approach promotes environmental sustainability and resource efficiency.

Chapter 4: Process Validation of the Downstream Processing of Lactic Acid Using a Fermented Substitute Feedstock.

Process validation (PV) is essential for licensing biopharmaceutical products like lactic acid. It covers three main areas: upstream processing (where fermentation or cell culture happens), downstream processing (where the product is recovered, purified, and modified if needed), and drug product manufacturing (which includes final packaging and preparation). PV studies build on earlier characterisation studies, showing a deeper understanding of the process. During early development, assays do not need full validation, but the methods used to monitor essential attributes must be shown to work well and be documented (Reifsnyder et al., 2011). This research was carried out to further validate the pH optimisation presented in **Chapter 2:** (**Publication #1**) and ensure the effective use of nanofiltration membranes for lactic acid permeability. An innovative substrate was treated through a series of membrane techniques. These techniques included microfiltration, nanofiltration pressure-driven membranes, and both monopolar and bipolar electrodialysis, aiming to obtain lactic acid efficiently.

The novel substrate (Table 2) was prepared consisting of a fermentation of candy waste and digestate (1:1) during 48 h in a 5-L bioreactor inoculated with 5 % (v/v) of *Enterococcus faecium* at pH 6.55±0.27 (Papadopoulou, Vance, et al., 2023). ***Publication #3***, "Separation of lactic acid from fermented residual resources using membrane technology" (Papadopoulou et al., 2023), discusses an innovative method to recover a solution containing a high-purity lactic acid from a low-cost, heterogeneous feedstock consisting of candy waste and digestate.

Table 2. Composition of the initial feedstock diluted in water 1:1 at pH 6.5

Composition	Concentration [g L^{-1}]
Total Solids (TS)	38.10±0.51
Volatile Solids (VS)	23.61±0.24
Glucose	n.d
Sucrose	n.d
Maltose	19.55±1.60
Lactic Acid	31.30±1.81
Succinic acid	0.30±0.30
Formic Acid	n.d.
Acetic acid	0.77±0.52

n.d.: not detected

The research ***Publication #3*** combines four membrane technologies (Figure 7), microfiltration, nanofiltration, monopolar and bipolar electrodialysis, with different configurations to optimise lactic acid recovery and minimise energy consumption.

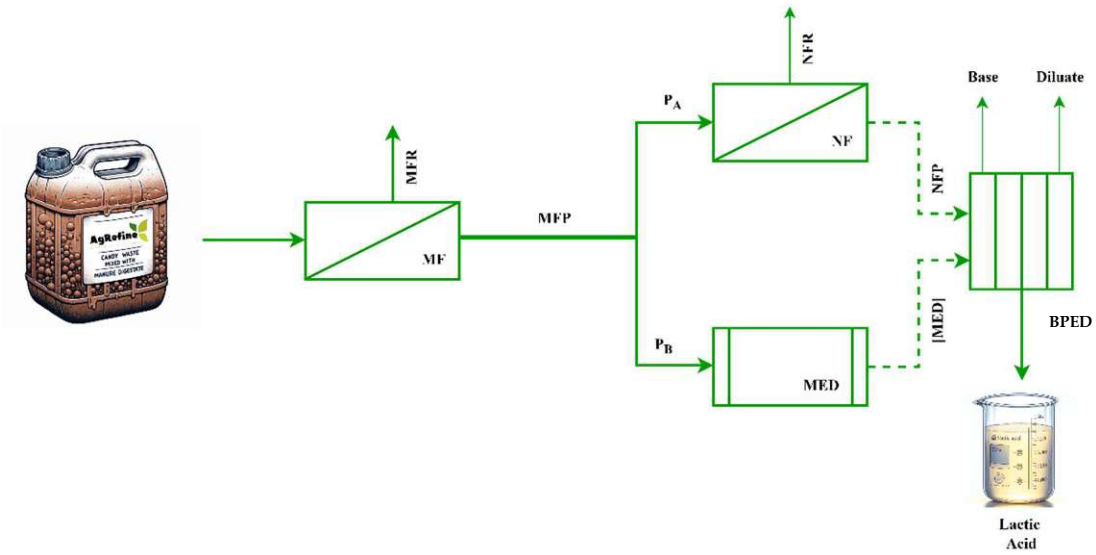

Figure 7. Graphical Abstract of the Process Revalidation using Candy Waste. (MF: Microfiltration, MFR: Microfiltration Retentate, MFP: Microfiltration Permeate, P_A: Process A, P_B: Process B, NF: Nanofiltration, NFR: Nanofiltration Retentate, NFP: Nanofiltration Permeate MED: Monopolar electrodialysis, BPED: Bipolar Electrodialysis).

Two processes were suggested in this research: Process A (P_a) and Process B (P_b). P_a consisted of treating the candy waste with MF, followed by sending the MF permeate to NF and then directing the NF permeate to BPED. On the other hand, P_b was treated with the same substrate, but after MF, the permeate was treated to MED, and then the MED concentrate was treated at BPED.

The downstream processing for candy waste was designed to involve electrodialysis (monopolar and bipolar) to improve the process and obtain a higher concentration of lactic acid. Electrodialysis (ED) is an advanced membrane technology with significant potential for concentrating ions from various aqueous waste streams like grass silage, candy waste and any aqueous residues. Usually, it removes organic acids from fermentation broths (Lipnizki et al., 2019). By integrating ED in both P_a and P_b, this research influences its efficiency in ion concentration to enhance the overall process of treating candy waste.

This ***Publication #3*** highlights the crucial role of regulating parameters such as pH to optimise membrane technologies for producing the desired bio-product. For lactic acid, the optimal pH values were found to be 2.8 for NF and 4.0 for monopolar electrodialysis (MED). Moreover, Process B, which combined MED with bipolar electrodialysis (BPED), achieved a 1.09-fold increase in lactic acid recovery compared to Process A, which combined NF with BPED. However, Process B also exhibited a specific energy demand 4.51 times higher than Process A, resulting in a 6.02-fold higher ion content in the final solution. Additionally, the application of fed-batch MED increased the lactic acid concentration from 43.70 to 114 g/L, demonstrating significant potential for industrial applications.

The process effectively separates a feed solution into an ion-rich concentrate and an ion-deficient diluate. This separation is achieved through an alternating arrangement of anion exchange membranes (AEM) and cation exchange membranes (CEM) combined with the application of direct current, forming adjacent concentrate and diluate zones. The process continues until the Limiting Current Density (LCD) is reached, a critical parameter dependent on the concentration gradient (Weisz et al., 2024).

The application ***Publication #3*** can demonstrate that membrane separation technologies effectively purify lactic acid from complex waste mixtures. Therefore, it contributes to waste valorisation in a biorefinery context. The optimisation presented regarding dropping the feedstock to pH 2.8 (Cabrera-González et al., 2022) to process it by nanofiltration is needed. Therefore, in ***Publication #3***, it is demonstrated that it improves the purification of lactic acid despite the feedstock.

Although this research shows new insight into a novel feedstock, additional areas could have been addressed, such as scale-up considerations, feasibility and sustainability of the process, ensuring they are cost-effective and environmentally friendly and capable of maintaining performance over time. Also, a comparison with other technologies could have been made.

Chapter 5: Analytics – Biosensor.

The concentration of metabolites, nutrients, and other critical quality attributes are essential for ensuring product quality and enabling effective process control. Despite this, there remains a significant gap in the measurements of critical parameters in the downstream process. This gap highlights the critical importance of speed and accuracy in downstream processing (Milewska et al., 2023).

The downstream processing can be monitored by process analytical technology, a system designed to design, analyse, and control manufacturing processes. It employs real-time measurements (Table 3) during processing to assess critical quality and performance attributes of raw and in-process materials (Shaikh et al., 2018). This approach aims to ensure the final product's quality by monitoring and managing these attributes throughout production.

Table 3. Measurements types in process analytical technology (Shaikh et al., 2018)

Measurement			
At line	**Online**	**Inline**	**Offline**
The sample is taken, isolated from the process stream, and analysed nearby.	The sample is diverted from the manufacturing process and can be reintegrated into the process stream.	The sample remains within the process stream and can be measured using invasive or non-invasive methods.	The sample is extracted from the process and analysed in a laboratory environment.

In the optimised downstream processing presented in this research thesis, High-Performance Liquid Chromatography (HPLC) is commonly used to characterise and quantify the chemical compounds from grass silage juice streams during lactic acid recovery through membrane technologies. This

offline technology, though time-consuming and expensive (Gupta et al., 2022), provides precise analysis of the sample components, ensuring quality and consistency in the recovered lactic acid. Despite its costs, HPLC's accuracy is essential for optimising the recovery process and maintaining product quality.

However, sampling errors can occur, such as instantaneous contamination, improper handling during sample preparation for HPLC, or technical issues like leaks, pressure ripples, artefact peaks, and peak shape distortion during measurement (Haidar Ahmad, 2017). These problems can compromise the accuracy and reliability of the analysis. Despite this, new technologies have been developed to measure the concentration of different compounds during downstream processing (J. B. Sweeney et al., 2018). One of the possibilities is to create new tools for inline technology, like a biosensor for immediate measurements (J. Sweeney et al., 2015, 2024; J. B. Sweeney et al., 2018). Inline technologies present an advantageous alternative, like compatibility with miniaturisation, robustness, high sensitivity and a wide detection range (Goker et al., 2020). Furthermore, it allows for instantaneous measurements during downstream processing, reducing the probability of such errors and enhancing the general performance and accuracy of the process.

A biosensor is a device that combines a biological sensing component with a transducer to produce a signal that is proportional to the concentration of a specific substance (Turner et al., 1987). Sweeney et al. (2018) developed a propionate biosensor by immobilising the *Escherichia coli* (*E. coli*) strain IMD Wldgypak, capable of metabolising propionate in concentrations ranging from 0.05 to 4.5 mM by being genetically modified. This biosensor detects propionate in synthetic leachates (SL) from anaerobic digestion. Leachate in this work is defined as a fermentation product from seaweed or grass that contains various organic acids (such as citric, lactic, acetic, butyric, succinic,

formic, and propionic acid), sugars (glucose, fructose and mannitol), and minerals (like NaCl, $MgSO_4$, KCl, among others).

Even though lactic acid is the primary analyte recovered in this research, the grass silage juice also contains other analytes considered impurities in this research (Table 1). Compounds such as propionic acid and succinic acid, though considered impurities in this context, are also studied within the AgRefine project as potential high-value molecules derived from biorefinery residues. In particular, succinic acid is a key focus (Grant Agreement 860477, 2019). The dual significance of succinic acid highlights its potential value, even as an impurity, and suggests further exploration of its applications in biorefining processes. To extend this research, a case study was conducted on a biosensor to detect succinic acid, showcasing its potential utility in these processes.

While the biosensor has been effectively created for specific propionate in SL, the effects of other impurities in the measurements, like salts, on this detection process remain unexplored. Furthermore, it is essential to acknowledge that salts found in SL may disrupt the activity of the microorganisms employed within the biosensor.

Gaffney et al., 2021 highlighted that the design of biosensors should be concentrated not only on their intrinsic properties, such as compound detection but also on their performance in challenging environments. These environments are characterised by extreme temperatures, toxic substances, and high levels of acidity and salinity, which are critical factors in assessing the long-term stability and effectiveness of the microorganisms used in the biosensors. The presence of salts in grass and seaweed silage may potentially influence the growth, cellular division, and genetic activity of the microorganisms in a biosensor. Consequently, the design of a biosensor for detecting organic acids should consider the impact of the salinity in the

sample. The salinity of the sample would influence the biosensor's halotolerance. Halotolerance refers to an organism's ability to tolerate salt concentrations exceeding those required for growing, and halotolerant microorganisms are considered when they survive at high-salt concentrations but do not need the conditions to prosper (Anton, 2015).

Halotolerance is essential to study because, for example, the seaweed *Alaria esculenta* and *Saccharina latissima* naturally contain mineral components, including sodium chloride (NaCl). Specifically, *A. esculenta* has a NaCl content of 1.6%, and *S. latissima* has 1.7%, as noted by (Sørensen et al., 2021). During the fermentation process or ensilage of seaweed, additional NaCl is added to the seaweed to inhibit the growth of unwanted microorganisms. This addition results in final NaCl concentrations of 2.5% for *A. esculenta* and 2.9 % for *S. latissima*. It is important to consider that NaCl concentration exceeding 3% (0.51 M) has been found to compromise *E. coli* viability, as per Doudoroff, 1940 research, which is comparably close to the NaCl levels found in silage from seaweed.

Another essential mineral that has to be considered is Mg^{2+}. Ometto et al., 2018 reported an elemental composition analysis of between 8,000 and 12,000 mg $kgDM^{-1}$ for *S. latissima* biomass, depending on the place of harvest.

However, Nepal & Kumar, 2020, reported that in a halotolerant of *E.coli*, cells were dead at a concentration of 1.25 M of $MgSO_4$ and exhibited morphological changes at 0.83 M. Given that magnesium is a significant constituent in *S. latissima*, as mentioned previously, its presence must be considered.

On the other hand, K^+ also plays a vital role in the biomass of *S. latissima*, reaching an elemental composition from 42,000 to 64,000 mg $kgDM^{-1}$ (Ometto et al., 2018). The effect of KCl on *E. coli* is reported to be at a concentration of 1.5 % (Abdulkarim et al., 2009), affecting the cells' growth but in a lower

concentration than NaCl. Thus, this element should also be measured to study its influence on biosensor detection.

In addition to developing a propionate biosensor, a succinic acid biosensor (Figure 8) is currently being developed and has not yet been reported. This work aims to evaluate the halotolerance characteristics of the succinic acid biosensor and the effect of three specific salts, potassium chloride (KCl), magnesium sulfate ($MgSO_4$) and sodium chloride (NaCl), on its performance and the difference of measurement regarding the measurement of just sample containing succinic acid.

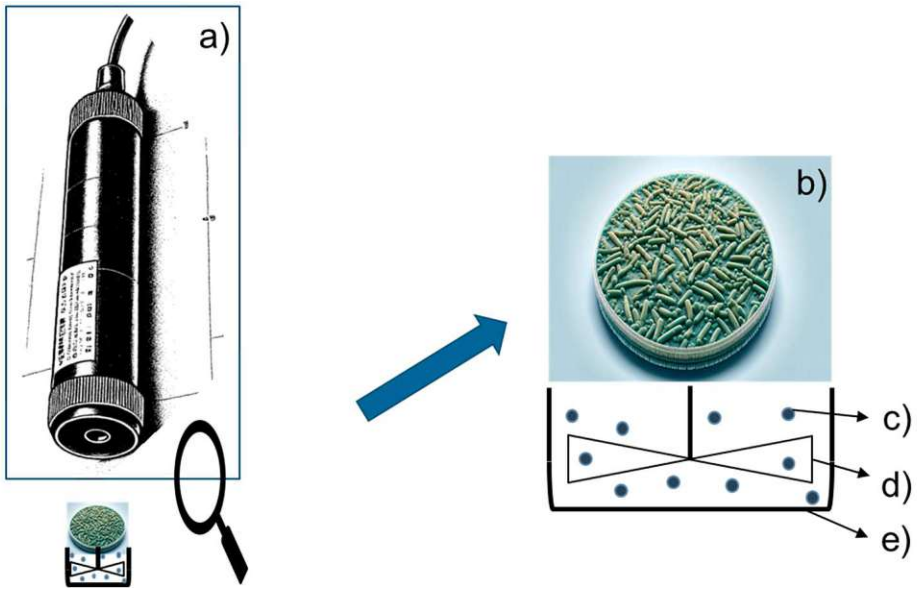

Figure 8. Biosensor design based on Sweeney et al., 2018. a) Vernier® DO-BTA probe, b) Microfiltration membrane 0.45 um containing microorganisms for SA detection, c) Model solution containing SA, d) Mixer (magnetic bar), and e) mini beaker.

5.1 Biosensor Fundamentals

5.1.1 Tricarboxylic acid cycle

The tricarboxylic acid cycle (TCA), also known as the Krebs or citric acid cycle, is a sequence of chemical reactions utilised by aerobic organisms (prokaryotes and eukaryotes) to produce energy. This energy generation occurs through acetyl-coenzyme A (CoA) oxidation, which is derived from fatty acids, carbohydrates and proteins (Choi et al., 2021).

The role of this process involves complex biochemical pathways to selectively uptake a specific organic acid into its metabolism. This study will be focused on succinic acid uptake.

Succinic acid (SA), also known as butanedioic acid ($C_4H_6O_4$), is a symmetrical dicarboxylic acid that contains four carbon atoms. It typically forms colourless, odourless crystals (Goldberg & Rokem, 2009). Naturally abundant in plants, animal tissues and various microorganisms. In biological systems, SA is synthesised during the TCA cycle (Table 4)under anaerobic conditions, where it is formed from α-ketoglutaric acid through the action of a α-ketoglutarate dehydrogenase (Goldberg & Rokem, 2009). The primary way to break down succinic acid in microorganisms or bacteria is the β-oxidation cycle, which involves multiple cycles where eve-chain acids are progressively converted into acetyl-CoA for further oxidation in the TCA.

The uptake of succinic acid into the cell (*E.coli*) is catalysed as follows (Swenson, 2018; Wei et al., 2023):

Table 4. TCA Cycle for succinic acid.

Chemical Reaction	**Catalysation Enzyme**
Succinate + FAD → Fumarate + $FADH_2$	Succinate dehydrogenase
Fumarate + H_2O→ Malate	Fumarase
Malate + NAD^+ → Oxaloacetate + NADH + H^+	Malate dehydrogenase
Oxaloacetate + Acetyl-CoA + H_2O → Citrate + CoA-SH	Citrate Synthase
Citrate ⇌ Isocitrate	Aconitase
Isocitrate + NAD^+ → Alpha-Ketoglutarate + NADH + CO_2	Isocitrate dehydrogenase
Alpha-Ketogrutarate + NAD^+ + CoA-SH → Succinyl-CoA+ NADH + CO_2	Alpha-Ketoglutarate dehydrogenase

Succinate is an essential circulating metabolite that plays a crucial role in regulating cellular nutrient metabolism. As an intermediate metabolite in the TCA cycle, it facilitates the continuous production of energy by being used as a substrate for succinate dehydrogenase. The energy produced by this cycle keeps the cellular function and maintains the cell metabolism (Wei et al., 2023).

5.1.2 Mathematical formulation

To efficiently estimate the millimolar (mM) concentration of biologically available succinate in a biological leachate sample, the following equation (Eq. 4) was used (J. B. Sweeney et al., 2022):

$$mM_{BL\ catabolite\ sample} = mM_{standard} \times \frac{mgO_2\ min^{-1}{}_{BL\ catabolite\ sample}}{mgO_2 min^{-1}{}_{standard}} \div mL_{BL\ catabolite\ sample} \times 20\ mL \quad \text{Eq. 4}$$

Where $mM_{standard}$ refers to the concentration of the standard solution, $mgO_2\ min^{-1}{}_{BL\ catabolite\ sample}$ represents the consumption rate of O_2 in the sample, $mgO_2 min^{-1}{}_{standard}$ is the consumption rate of O_2 of the standard and $mL_{BL\ catabolite\ sample}$ denotes the volume of the sample. 20 mL is the total working volume.

While the formula is provided, raw voltage signal (mV s^{-1}) data will be illustrated due to the requirement for a conversion factor from mV s^{-1} to mg O_2, which is protected by the patent (J. Sweeney et al., 2024).

5.2 Experimental Design of the Biosensor System

5.2.1 Biosensor

As reported by J. B. Sweeney et al., 2022, the dissolved oxygen in the samples was measured using a Vernier® DO-BTA probe (Bearverton, OR, USA) every 30 minutes. Microorganisms were deposited onto the surface of a 0.45-um cellulose membrane (GE Healthcare) by vacuum filtration. This membrane was then affixed to the probe tips with parafilm wrap. The raw voltage data from the probe were acquired using Vernier's Arduino interface.

5.2.2 Chemical Solution Samples

The biosensor was successfully previously tested for succinic acid in synthetic solutions and grass silage. Therefore, four different synthetic

solutions were prepared to test the biosensor again, simulating the seaweed silage's environmental conditions regarding salinity (described in Chapter 5:).

The concentrations of each chemical compound in the solution are given in Table 5. Salts are defined as a mixture of KCl, NaCl and $MgSO_4$. Solution one, SA 1000, consists only of $C_4H_6O_4$. The solution two, SA 1000 + Salts, contains $C_4H_6O_4$, KCl, NaCl and $MgSO_4$. The solution three SA 1000 + Salts + PO_4^{3-} + pH 5 is composed of $C_4H_6O_4$, KCl, NaCl, $MgSO_4$, and Na_3PO_4 with a pH adjusted to 5 with HCl. Finally, solution four contains exactly the same compounds as the third solution, except for pH adjustment.

Table 5. Concentration of each chemical compound in the solution.

Chemical Compound	**Concentration [g L^{-1}]**	**Manufacture**
Succinic Acid ($C_4H_6O_4$)	5	Sigma-Aldrich
Potassium Chloride (KCl)	8	Sigma-Aldrich
Sodium Chloride (NaCl)	30	Sigma-Aldrich
Magnesium Sulfate ($MgSO_4$)	20	Sigma-Aldrich
Sodium Phosphate (Na_3PO_4)	3	-

Every solution was tested using the biosensor, and statistical analysis was carried out after 40 hours.

5.3 Results

5.3.1 The effect of a mixed salt solution on the reading of the biosensor, statistical analysis.

A statistical analysis was performed to evaluate the effect of the salts in the response to oxygen consumption rate. Figure 9 shows the oxygen consumption rate, measured in millivolts per second [mV s^{-1}], of the four different samples throughout 40 h. Each curve belongs to a different experimental condition (solution one, two, three and four). The curve SA 1000 is the baseline for the comparison.

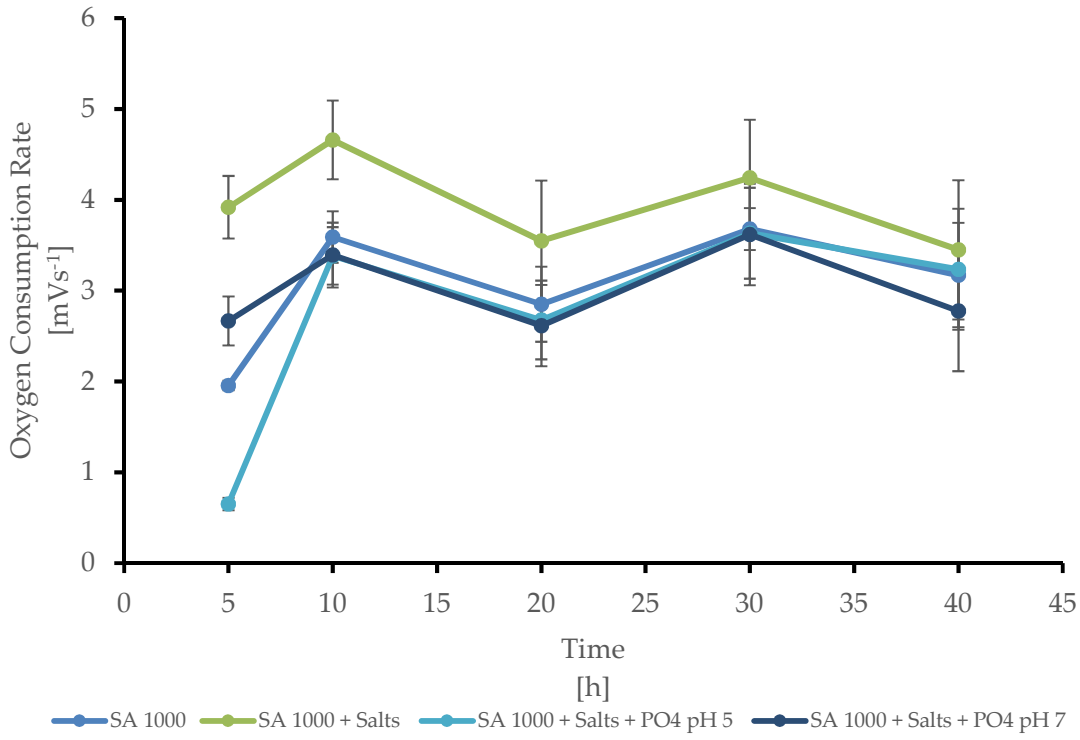

Figure 9. Biosensing responds to succinic acid samples mixed with different salts.

This experiment aims to compare the effect of the salt addition on the baseline condition SA 1000, having as a null hypothesis that the salt addition in the sample and pH do not influence the measurements of the oxygen consumption rate. A One-Way Analysis of Variance (ANOVA) was performed to compare SA 1000 vs SA 1000 + Salts, SA 1000 vs SA 1000 + Salts + PO_4^{3-} pH 5, and SA 1000 + Salts + PO_4^{3-} pH 7 using the data in Table 6. At the same time, comparison between SA 1000 + Salts vs SA 1000 + Salts + PO_4^{3-} pH 5, SA 1000 + Salts vs SA 1000 + Salts + PO_4^{3-} pH 7, and SA 1000 + Salts + PO_4^{3-} pH 5 vs SA 1000 + Salts + PO_4^{3-} pH 7.

Table 6. Oxygen Consumption Rate [mVs^{-1}]

Time [h]	**SA 1000 (Baseline)**	**SA 1000 + Salts**	**SA 1000 + Salts + PO_4^{3-} pH 5**	**SA 1000 + Salts + PO_4^{3-} pH 7**
5	1.96±0.05	3.92±0.35	0.65±0.07	2.67±0.27
10	3.59±0.28	4.66±0.43	3.38±0.32	3.39±0.36
20	2.85±0.41	3.55±0.67	2.68±0.43	2.62±0.45
30	3.68±0.23	4.24±0.64	3.63±0.50	3.62±0.56
40	3.17±0.57	3.45±0.77	3.24±0.67	2.78±0.66

This research aimed to compare the effect of the salt addition in a succinic acid solution when the biosensor measures the oxygen consumption rate. The baseline condition is SA 1000; however, a comparison between all of the measurements was carried out. A one-way ANOVA statistical analysis showed significance and no significance when comparing Table 7.

Table 7. ANOVA results, $p<0.05$

Comparison	F-value	p-value	Significance
SA 1000 vs. SA 1000 + Salts	5.68680	0.04422	Yes
SA 1000 vs. SA 1000 + Salts + PO_4^{3-} pH 5	0.28727	0.60655	No
SA 1000 vs. SA 1000 + Salts + PO_4^{3-} pH 7	0.00926	0.92571	No
SA 1000 + Salts vs. SA 1000 + Salts + PO_4^{3-} pH 5	4.56262	0.06518	No
SA 1000 + Salts vs. SA 1000 + Salts + PO_4^{3-} pH 7	9.77479	0.01409	Yes
SA 1000 + Salts + PO_4^{3-} pH 5 vs. SA 1000 + Salts + PO_4^{3-} pH 7	0.26630	0.619785	No

The SA 1000 + Salts conditions demonstrated a significant difference from the baseline, with a p-value of 0.044, indicating that adding salts had a notable impact on the measurement values. However, more studies are needed, as this p-value is near 0.05. On the other hand, the addition of PO_4^{3-} independently, if the pH is adjusted, shows no statistically significant differences when compared to SA 1000. When pH is 5, the p-value is 0.61, while pH 7 is 0.93, it means the mixture of salts and phosphate does not influence the measurements regarding the baseline, highlighting that the only sample that has statistical significance is the SA 1000 + Salts. On the other hand, the change in pH does not influence the oxygen consumption rate measurements. At the same time, the two measurements regarding pH were compared among them, where there were no significant differences as the p-value was 0.07.

The results suggest that when PO_4^{3-} is added to the highly concentrated salt mixture, the *E. coli*, genetically modified, can consume similar oxygen in a

sample without any salt. Therefore, besides the selective recognition of succinic acid, *E. coli* is classified according to its halotolerance as a slight halophile (Gaffney et al., 2021; Wang et al., 2023) and consequently the biosensor can be utilised for seaweed silage samples measurements.

Chapter 6: Perspective of a simplified model for circular economy in extreme conditions.

The project AgRefine is dedicated to equipping the next generation of innovators in the Circular Economy with the essential skills required for their roles. The sustainable utilization of natural resources within AgRefine requires a comprehensive approach, engaging key stakeholders such as farmers, consumers, regulatory bodies, and scientists. In addition, AgRefine offers the platform for developing innovative, sustainable technologies and profitable green business practices aimed at managing agricultural waste, by-products, and coproducts. Furthermore, it explores valorisation pathways for resources specific to coastal areas, promoting efficient resource use and sustainability (Grant Agreement 860477, 2019).

Considering these statements in the grant agreement, two of the Early Stage Researchers from coastal areas have proposed a simplified model for extreme environmental conditions like the Atacama and Sonoran Desert. This model also considers an entirely different type of environment in comparison to Europe, allowing the developed technologies within the AgRefine project to be applicable across diverse settings.

Feedstock availability for biorefinery processes is mainly based on geographical conditions; for that reason, ***Publication #2,*** "Development of a Model for the Implementation of the Circular Economy in Desert Coastal Regions", proposes the development of a circular economy in extreme conditions. In this kind of environment, high UV radiation, non-arable lands, and seawater offer a wide range of possibilities that have not been broadly studied in applying biorefinery in extreme conditions. ***Publication #2*** explores the feasibility of implementing a simplified circular economy model specially designed for arid coastal areas like Atacama and the Sonoran Desert.

The model focuses on water desalination, considering the massive availability of solar energy and the impact of the brine produced during water purification. Solar energy availability is considered an essential resource for energy production using solar panels, as Chile is one of the leaders in solar energy consumption. Moreover, the accessibility of non-arable lands is considered an advantage for microalgae production, which can be derived from biochemical compounds like proteins, lipids, or sugars. In addition, the location next to the sea is another advantage that can be utilised to cultivate seaweed, a scarcely studied renewal resource. However, the management of waste and residues for these technologies must also be considered and therefore, an implementation of an anaerobic digestion plant is proposed.

The potential benefit of ***Publication #2*** is that if it is implemented successfully, this model could significantly improve resource efficiency, reduce environmental impacts and support the sustainable development of desert coastal communities.

Even though ***Publication #2*** offers an overview of "what if", it lacks empirical data and cases of studies, cost-benefit evaluation, sustainability metrics like carbon footprint, scalability and adaptability, technological readiness and a detailed consideration of the social implications that include, for example, job creation, required skills, impact and practice on the local culture, all of these limitations, could contribute to having a real scenario about implementing these technologies in a coastal arid region.

Chapter 7:Conclusions and Outlook

This dissertation provides a comprehensive evaluation of lactic acid purification using a model solution, grass silage, and candy waste using membrane technology, focusing on its integration into sustainable practices. The overall research study in this thesis (***Publication #1, #2, #3, and submitted #4***) explores the efficiency of nanofiltration and biorefinery process optimisation for effective lactic acid separation and the use of the retentates for microalgae cultivation. Additionally, it incorporates analytical chemistry to evaluate downstream processing via standard methods and an innovative inline biosensor technology for potential process monitoring. Furthermore, this research proposes a circular economy model, applying developed lab-scale technologies to extreme environmental conditions like the Atacama and Sonoran deserts.

Publication #1 concludes that pH and membrane type significantly influence lactic acid permeability during nanofiltration. Operating under acidic conditions, with pH levels below the pKa of LA, clearly improves permeability. Measurements of pH and conductivity during the process in both permeate and retentate help to provide a comprehensive overview of LA permeability. Additionally, evaluating rejection and flux is essential for improving downstream processing and enabling industrial scale-up.

Screening commercially available nanofiltration membranes with different molecular weight cut-offs offers valuable insights for designing future pilot-scale or industrial processes. Furthermore, the detailed data obtained from these screenings can be used for modelling and simulation, helping predict process performance based on lab-scale information.

Membrane technologies offer promising solutions for efficient contaminant removal and environmentally friendly processing methods. Exploring various membrane materials and configurations is crucial for enhancing permeability and selectivity to improve LA separation further. This research underscores the potential to meet the projected global LA demand of 1845 kt by 2022. Future studies should also consider the environmental and economic impacts of industrial-scale processes.

To achieve sustainable LA recovery, optimising the applied pressure in downstream processing is essential to reduce energy consumption. Moreover, the investigation of evaluating different lactic acid concentrations contained in a solution should be carried out to understand the influence of these on the separation process. Also, innovations in membrane fabrication through techniques like electrospinning and precise control of operating conditions are crucial in enhancing overall efficiency and effectiveness. These advancements will support a competent scale-up and broader industrial applications in bioplastics, food, and pharmaceuticals.

Conversely, ***Publication #3*** initiated using a novel mixed substrate of candy waste and digestate for microbial fermentation to produce lactic acid, a combination that had not been previously explored. Lab-scale experiments revealed that specific process routes configurated as MF, NF, and BPED or MF, MED, and BPED significantly enhance LA recovery and purity while minimising energy consumption. The results demonstrate the viability of converting high-sugar industrial residues into valuable bioproducts, suggesting a sustainable and potentially economically feasible pathway for LA production. Additionally, these findings open new options for industrial-scale applications, highlighting the possibility of reducing waste and energy use simultaneously. Furthermore, exploring additional sugar-rich waste substrates (for example, from soft drinks, marmalade, jelly manufacturers, and

more) to expand the scope and impact of sustainable LA production could represent a chance to improve economic prospects in the industry by valorising waste by fermentation for further purposes; however, it has to be deeply researched.

Besides, the recovery of a side stream mainly contained maltose during downstream processing, particularly in the retentates, represents a potential new source for secondary fermentation. This side stream could also be purified as a valuable by-product. Still, further studies are needed to fully explore and optimise these possibilities, ensuring efficient integration into existing processes and maximising overall resource utilisation.

Furthermore, ***Publication #4*** demonstrated that utilising streams from the downstream processing of grass silage to cultivate microalgae is an innovative approach that closes the loop in the downstream processing of lactic acid from grass silage juice. Using grass silage juice permeates and retentates (secondary effluents) from lactic acid production through membrane filtration is a sustainable and theoretically cost-effective approach for microalgae cultivation and further purification. However, a life cycle assessment should be done to achieve this statement. This finding suggests that microalgae cultivation can be carried out by using these streams as a culture medium. Additionally, cultivating *Chlorella vulgaris* in the nanofiltration permeate, which contains a high concentration of lactic acid and a low concentration of acetic acid, could be an option for a supplementary lactic acid bio-purification step. This is because chlorella is not known as a lactic acid consumer but as an acetic acid, and it may consume other molecules, hypothetically resulting in a purer lactic acid stream after cultivation. Nevertheless, there is still a research question to be studied: Does *Chlorella vulgaris* offer an alternative for lactic acid purification to conventional purification methods like evaporation or crystallisation?

Moreover, the ***unpublished*** and ***not-submitted*** research (***Chapter 5:***) biosensors propose real-time monitoring, which is crucial for accurately determining the concentration of specific compounds during a purification process. The approach of using whole-cell biosensors, tested across various substrate combinations, can be broadly applied to samples that contain succinic acid and samples with high salt content, like seaweed silage. The genetic modifications demonstrated specificity for the target compounds and showed no interference in high-salinity environments. The biosensor's fast response could positively impact the cost of chemical analysis, but this has to be deeply studied.

Finally, ***Publication #2*** shows a perspective on implementing a circular economy model, incorporating micro and macroalgae cultivation, nutrient recovery, water desalination, and improvement of wastewater treatment. This model aims to address environmental sustainability in arid regions by adapting different technologies developed in the AgRefine project but under extreme conditions. Combining technologies such as integrating anaerobic digestion, using CO_2 for algae cultivation, and recovering nutrients for hydroponics could result in a highly synergistic approach. However, the lack of an economic assessment and a proper feasibility study means that further work is needed to develop an improved model. This publication also highlights that while substrates for high-value products may not always be available, there is potential for valorising other effluents, such as brine from water desalination or the products from anaerobic digestion. Moreover, the "luck" of having high radiation in regions like the deserts of Mexico and Chile may result in low-cost energy production, providing an advantageous and environmentally friendly solution. The challenges posed by the lack of arable land necessitate rethinking climate change strategies, particularly by examining extreme conditions.

Overall, the entire project, including the use of microfiltration and nanofiltration membranes, electrodialysis, and microalgae cultivation using retentates and monitoring the whole process via a biosensor, presents a promising scenario of circular economy applications. This approach holds significant potential for industrial implementation. Additionally, the integration of modelling, simulation, and scalability analysis will provide valuable insights when lab-scale data is available. Consequently, this research offers a comprehensive dataset of novel technologies, enhanced downstream processing and a framework for future industrial applications.

Chapter 8:Scientific Articles.

- ***Publication #1***:

Evaluation of Nanofiltration Membranes for Pure Lactic Acid Permeability
Mayuki Cabrera-González, Amal Ahmed, Khaled Maamo, Mohammad Salem, Christian Jordan, Michael Harasek.
Membranes 2022, 12(3), 302.
https://doi.org/10.3390/membranes12030302

- ***Publication #2***:

Development of a Model for the Implementation of the Circular Economy in Desert Coastal Regions
Mayuki Cabrera-González, Fernando Ramonet, Michael Harasek.
Land 2022, 11(9), 1506.
https://doi.org/10.3390/land11091506

- ***Publication #3***:

Separation of Lactic Acid from Fermented Residual Resources using Membrane Technology.
Eleftheria Papadopoulou, **Mayuki Cabrera-González,** Daniela Reif, Amal Ahmed, Panagiotis Tsapekos, Irini Angelidaki, Michael Harasek.
Journal of Environmental Chemical Engineering, 2023, 11(5), 110881.
https://doi.org/10.1016/j.jece.2023.110881

- ***Publication #4*** (Submitted):

Production of *Chlorella vulgaris* using grass silage juice and secondary effluents from lactic acid recovery through pressure-driven membranes
Mayuki Cabrera-González, Marcella Fernandes de Souza, Erik Meers, Amal Ahmed, Michael Harasek.
Journal of Algal Research

membranes

MDPI

Article

Evaluation of Nanofiltration Membranes for Pure Lactic Acid Permeability

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Abstract: Lactic acid (LA) is an organic acid produced by fermentation or chemical synthesis. It plays a crucial role in the pharmaceutical, food and plastic industries. In the fermentation of, for example, grass silage, LA and different compounds are produced. To purify lactic acid, researchers have tried to investigate membrane technology to achieve a high yield of lactic acid permeance. This study tested four commercially available nanofiltration membranes (NF270, MPF-36, Toray NF, and Alfa Laval NF). Nanofiltration experiments were performed to investigate the rejection levels of lactic acid from a binary solution by using distinct molecular weight cut off membranes. All of the experiments were conducted with a lab-scale cross-flow membrane unit. Different operating conditions (pH, temperature) were studied for each membrane; the optimal process condition was found at 25 °C and pH 2.8. With higher temperatures and pH, an increase in LA rejection was observed. The MPF-36 membrane shows the lowest lactic acid rejection yield of 7%, while NF270 has the highest rejection yield of 71% at 25 °C and pH 2.8. These results will be helpful in the future to understand both the interaction of lactic acid permeance through nanofiltration membranes and process scale-up.

Keywords: lactic acid; nanofiltration; membranes

Citation: Cabrera-González, M.; Ahmed, A.; Maamo, K.; Salem, M.; Jordan, C.; Harasek, M. Evaluation of Nanofiltration Membranes for Pure Lactic Acid Permeability. *Membranes* **2022**, *12*, 302. https://doi.org/10.3390/membranes12030302

Academic Editors: Sotiris I. Patsios, Konstantinos V. Plakas and Dimitris C. Sioutopoulos

Received: 15 December 2021
Accepted: 6 March 2022
Published: 8 March 2022

1. Introduction

Lactic acid (LA) is an essential chemical compound used as a flavour, acidifier, and preservative in the food industry. The pharmaceutical, cosmetic and polymers industries use lactic acid as a raw material to develop commercial products [1]. Lactic acid is produced in two ways: fermentation (biotechnological process) and chemical synthesis. Different feedstocks have been utilised for lactic acid production to replace the oil-based material. For example, green biomass, like grass or seaweed, can be fermented to obtain lactic acid [2]. The fermentation process for lactic acid production is performed by lactic acid bacteria (LAB) through metabolic pathways. LAB, such as *Lactobacillus delbrueckii* [3] or *Bacillus coagulants* strains A20, A369, A107, and A59 [4], can convert sugars like fructose, glucose, arabinose, etc., into lactic acid, ethanol, butyric, propionic, acetic, and caproic acid, and other organic acids [5]. Although fermentation has many advantages, the production of other chemical compounds besides lactic acid is not desirable in the industries mentioned above, since they require a pure form of this compound (LA) [6]. Therefore, LA without impurities or in a highly refined form is mandatory for industrial application [7].

Even though the molecular compounds generated in the fermentation are potentially valuable products, downstream processing steps are necessary to purify and recover lactic acid and to remove the undesired compounds.

Downstream processing (DP) is a series of unit operations that remove most of the impurities from a complex solution to obtain a set of pure chemical compounds in different stages of the entire process. All of the required steps in DP establish an expensive process

to recover lactic acid from any feedstock, and it can cost between 50% [8] and 80% of the total production [9]. A conventional route for lactic acid recovery goes from fermentation to extraction, then distillation, after that adsorption to go through membrane filtration, to evaporation and to end with a crystallisation [10]. Therefore, the typical route can be replaced with selective membranes to recover lactic acid. Membrane technologies are used in the downstream processing of chemical and biological industries [11]. The advantages of membranes are that they are highly selective, have high levels of purification, can be integrated into conventional fermenters and reactors, and are flexible in the scale of production [12]

Nanofiltration (NF) is a membrane separation technique situated between ultrafiltration and reverse osmosis. The nominal molecular weight cut-off (MWCO) of NF is in the range of 200 to 1000 g mol^{-1} [13]. NF is ideal for purifying lactic acid as there is no need to use additional chemicals [14]. According to the cost–benefit and selectivity, the nanofiltration separation process is more competitive than conventional separation. In addition, the high rejection of small organic molecules and multivalent inorganic salts at modest applied pressures are some of the essential advantages of NF [15].

The importance of nanofiltration membranes technology has increased in many industries, specifically biotechnology, in the last decade. NF membranes are used in downstream processing because they separate proteins, nutrients, cells, unconverted carbon sources, and salts [16] from the fermented broth.

Several authors have addressed the separation of lactic acid from complex solutions (acid whey, sugar bread, and crust bread, among others.) [6,17–19]. However, there is no extensive research for nanofiltration on a binary solution of lactic acid. The study of the binary solution of lactic acid in the membrane process will allow to understand the transport phenomena of this molecular compound through nanofiltration [20].

One of the critical parameters in transport phenomena is mass transfer. This nonequilibrium process involves driving forces: electrical potential, temperature, concentration and pressure, selective sorption, mechanical sieving, and diffusion through the membranes [21].

Diffusion plays a vital role in chemical processes, such as porous catalysis, across phase interfaces and porous membranes, within fluids and gels. The diffusion coefficient is a key parameter to design mass transfer and membrane performance evaluation [22].

The Equation of Maxwell–Stefan describes the mixture transport of a binary or multicompound solution to predict the separation performances through membranes based on the solution-diffusion model [23]. Therefore, experimental work needs to be conducted to use and support this model for simulation purposes.

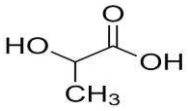
This research aims to study the specific permeance of lactic acid as a binary solution in four different commercially available membranes. In addition, the effect of pH, temperature, and membrane pore size in the permeance of lactic acid were investigated. This is a preliminary experimental investigation of the retention of lactic acid in NF. The obtained data will be helpful to understand the interactions between LA and membrane properties at different pH and temperatures. In addition, to gain an overview to help choose the best membrane performance for lactic acid permeability for future downstream processing.

2. Materials and Methods

2.1. Preparation of the Lactic Acid Solution

Lactic acid ($C_3H_6O_3$; ≥85%, Sigma-Aldrich, Wien, Austria) was used as a raw material to prepare the binary solution in this work. First, 50 g of LA were dissolved in 2 L of deionised water, at room temperature in an air atmosphere. The final concentration for $C_3H_6O_3$ was 0.277 mol L^{-1}. This concentration is based on green silage juice [24]. The pH of the initial solution was 2.8, and then it was adjusted to 3.9 and 6.0 by adding 7 and 14 g of NaOH, respectively. The pH was adjusted to approach the pH of grass silage (Zhao et al., 2021). The physicochemical properties of lactic acid are presented in Table 1.

Table 1. Physicochemical properties of the lactic acid.

Property	Value
Molecular structure	
Molecular formula	$C_3H_6O_3$
Molecular weight g mol^{-1}	90.08
Dissociation constant (pKa) at 25 °C	3.86
Dissociation constant (pKa) at 40 °C	3.67
Diffusion coefficient at 30 °C [25]	11.2×10^{-10} m^2 s^{-1}

2.2. Experimental Set-Up and Nanofiltration Membranes

The separation performance of NF270, MPF-36, Toray NF, and Alfa Laval NF commercially available flat sheet membranes were evaluated separately in the nanofiltration of the lactic acid solution. A lab-scale cross-flow filtration membrane unit, model OS-MC-01 (Figure 1), was used to carry out the experiments. The unit is equipped with a 2 L capacity stainless steel jacketed feed tank. The feed solution is pumped to the rectangular cross-flow membrane module, with an effective membrane area of 0.008 m^2 (0.04 m × 0.2 m), through a CAT-high pressure piston pump model 231, with a maximum flow capacity of 3.7 L min^{-1} and a pressure up to 60 bar. All of the experiments were conducted in a batch concentration mode; the retentate was recycled back to the feed tank, and the permeate was continuously exiting the system.

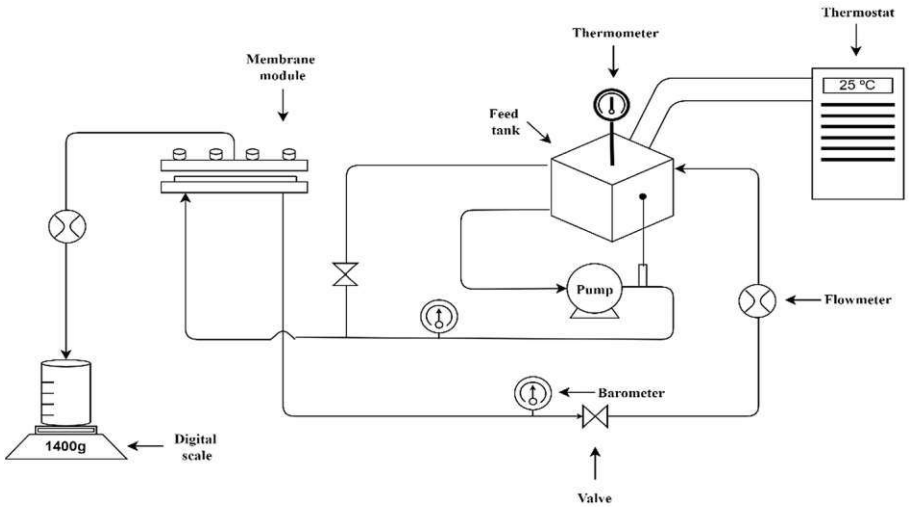


Figure 1. Schema of membrane test cell (model OS-MC-01).

The four nanofiltration membranes (Table 2) were chosen according to the different molecular weight cut-off (MWCO). To determine the permeance of LA and the performance of each membrane, samples of the permeate and the retentate were taken at the end of the nanofiltration process.

The nanofiltration process finished when there was 1400 g in the permeate, the remaining 30% of the solution was left in the feed tank to take the retentate samples for concentration analysis and to avoid the dry run of the pump. The permeance of the LA is directly related to the rejection of LA. The concentration of LA in the permeate and retentate was detected by HPLC.

Table 2. Characteristics of the nanofiltration membranes.

Parameter	NF270	SelRO® MPF-36	Toray NF	Alfa Laval NF
Manufacture	FilmTec™	Koch	Toray	Alfa Laval
Material	Polypiperazine	Polysulfone	Polypiperazineamide	Polyamide
MWCO (g mol^{-1})	200	1000	200	300
Maximum operating temperature (°C)	45	60	50	50
Operating pH range	3–10	3–10	3.5–10.5	3–10
Max operating pressure (bar)	41	35	55.2	55
Isoelectric point (pH)	3.6 [26]	5–6.5 [27]	4.0	4.0

Before the experiment, all the membranes were hydrated by being inserted in deionised water for 20 min before use. Then, the membranes were compacted in the module for 20 min more under pressure at 32 bar and a 3.6 L min^{-1} cross-flow rate.

2.3. Operating Conditions

The experiments were carried out using the solution mentioned in Section 2.1. The nanofiltration process evaluated two independent variables (pH and temperature) to determine their effect on lactic acid permeance and concentration. Table 3 presents the operating conditions which were applied for each membrane. The following parameters were calculated for each membrane: water flux at the beginning and the end of every experiment, the retention coefficients of lactic acid, and permeate flux. A VWR thermo-bath controlled the temperature during the experiments. Conductivity, permeate flux, and pH were measured every 10 min until 70% of the model solution was collected. A total of 16 experiments were carried out.

Table 3. Experimental conditions for lactic acid permeability.

Experiment	Pressure (bar)	Temperature (°C)	pH	Lactic Acid (g L^{-1})
1	32	25	2.8	25
2	32	40	2.8	25
3	32	25	3.9	25
4	32	25	6.0	25

The osmotic pressure of the feed in the binary solution containing the lactic acid was 7 bar. During the batch mode, the concentration in the feed tank increases with time due to the solvent removal, which leads to the increased osmotic pressure of the solution; therefore, the applicable constant driving force at high pressure was 32 bar to avoid flux reduction. The membranes used in this study are permeable for water at high pressure. The temperature of nanofiltration was chosen according to the biomass fermentation at 40 °C for lactic acid production [28]. Regarding 25 °C, the temperature was used to compare the rejection of lactic acid at room temperature.

2.4. Lactic Acid Quantification

The concentration of LA in the feed, permeate, and retentate was quantified by High-Performance Liquid Chromatography (HPLC). All the samples were diluted to 1:8 to match the HPLC detection range. The method used in the HPLC is shown in Table 4.

Table 4. The method used in the HPLC.

Experiment	Value
Equipment	Shimadzu UFLC
Flow (mL min^{-1})	0.6
Injection volume (μL)	10
Mobile phase of H_2SO_4 (mM)	5
Gradient	Isocratic
Oven temperature (°C)	50
Refractive index detector	RID-10A
column	Shodex SH1011 (8 × 300 mm)
Guard column	SH-G Sugar

The rejection of lactic acid was calculated from Equation (1) to determine the performance of the nanofiltration membrane. C_p and C_f are the concentrations in the permeate and the feed, respectively.

$$R = \left(1 - \left(\frac{C_P}{C_f}\right)\right) \times 100\% \quad (1)$$

3. Results and Discussion

3.1. Water Flux and Flux Reduction

Pure water flux is one of the parameters used to describe membrane characteristics [29]. In the separation process, the feed solution affects the performance of the membranes in terms of flux. The particles or colloids interact physically with the membrane, which causes a pore or surface layer blocking [30]. Organic substances can produce flux reduction because they can be attached via adsorption in the membrane. On the other hand, inorganic compounds can also form membrane blocks because they can precipitate dissolved components due to oxidation or pH variation [30]. Figure 2 presents the pure water flux obtained from the four nanofiltration membranes at different experimental conditions (Table 3). The following Equation (2) calculates the flux reduction:

$$FR_{PWF}(\%) = \frac{PWF_b - PWF_a}{PWF_b} \times 100\% \quad (2)$$

FR_{PWF} is the flux reduction in the pure water flux%, PWF_a is the pure water flux after the LA filtration in Kg m^{-2} h^{-1}, and PWF_b is the pure water flux before the LA filtration in Kg m^{-2} h^{-1} [31].

The highest water flux was for NF270, MPF-36, Toray NF, and Alfa Laval NF at 40 °C, which exhibited a flux of 520, 372, 292, and 320 Kg m^{-2} h^{-1}, respectively, before the filtration of the binary solution.

After the nanofiltration of a lactic acid binary solution, no flux reduction occurred when Toray NF was used in experiment 1 (Figure 2a) and experiment 4 (Figure 2d), as well as in Alfa Laval in experiment 2 (Figure 2b), because the FR_{PWF} is 0%. In this case, it can be assumed that there is no effect on the surface of the membrane from the filtration of the LA solution. The most affected membrane with the highest flux reduction was NF270 in experiment 3 (Figure 2c) and experiment 4 (Figure 2d), with a FR_{PWF} of 15% on average.

In addition, no flux reduction was observed for MPF-36 for pH 6.0. On the other hand, the membrane NF270 had a decreasing flux at pH 3.9 and 6.0; in both cases, the water flux diminished by 15% regarding the FR_{PWF} for this membrane. Even though the NF270 presented the highest water flux compared to the other membranes used in this study, this membrane experienced the most flux reduction. Figure 3 represents a 3D image of NF270 after being tested for LA permeability, measured by a 3D laser-scanning microscope (Keyence VK-X3000 Series) to observe the change in the structure of the membrane. This finding is concordant with [32], who found the same decline in flux for NF270 compared to this study.

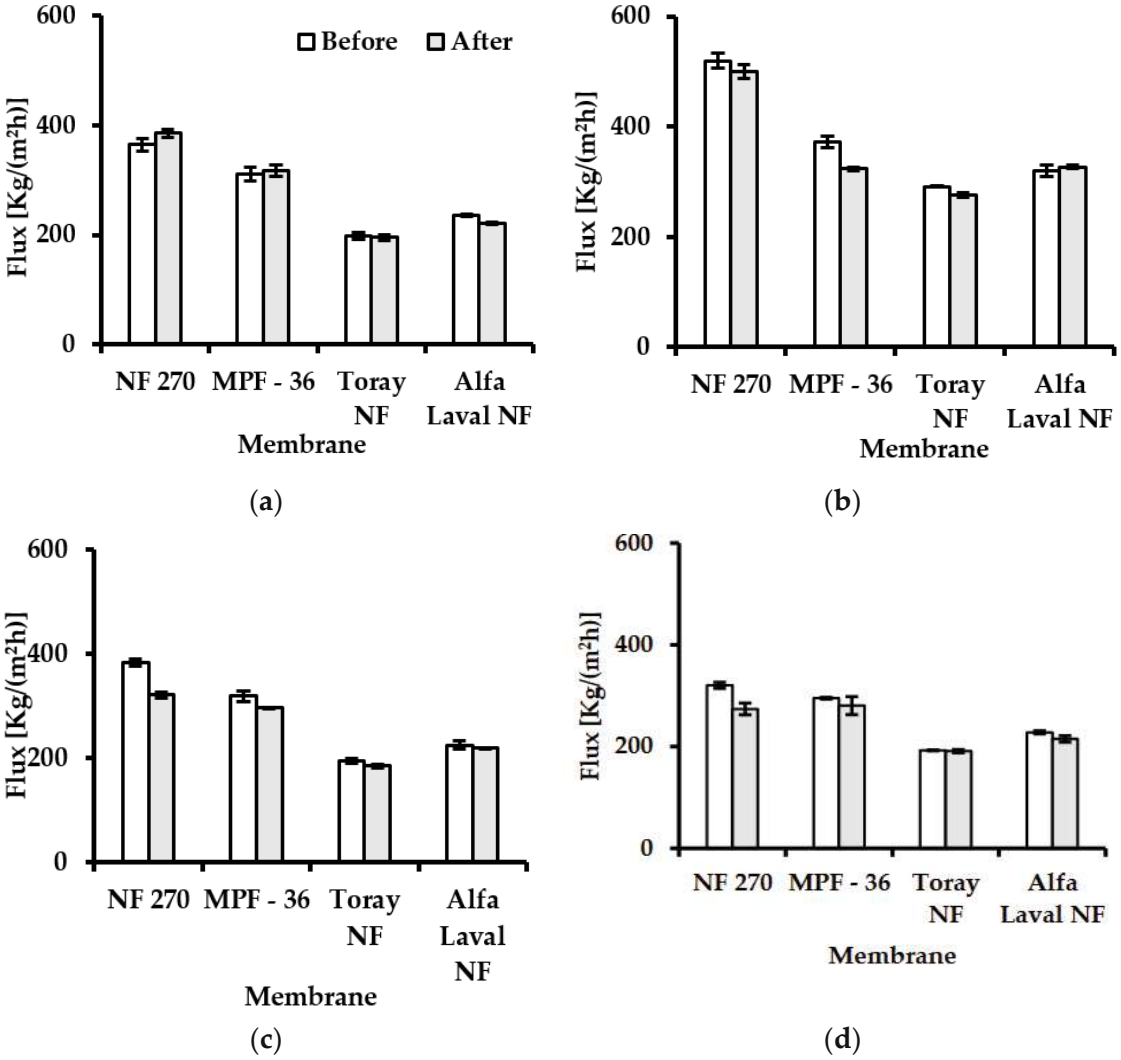


Figure 2. Water flux before and after the experiment with lactic acid for NF270, MPF-36, Toray NF, and Alfa Laval NF membranes. (**a**) at pH 2.8, T: 25 °C and 32 bar. (**b**) at pH 2.8, T: 40 °C and 32 bar. (**c**) at pH 3.9, T: 25 °C and 32 bar. (**d**) at pH 6.0, T: 25 °C and 32 bar.

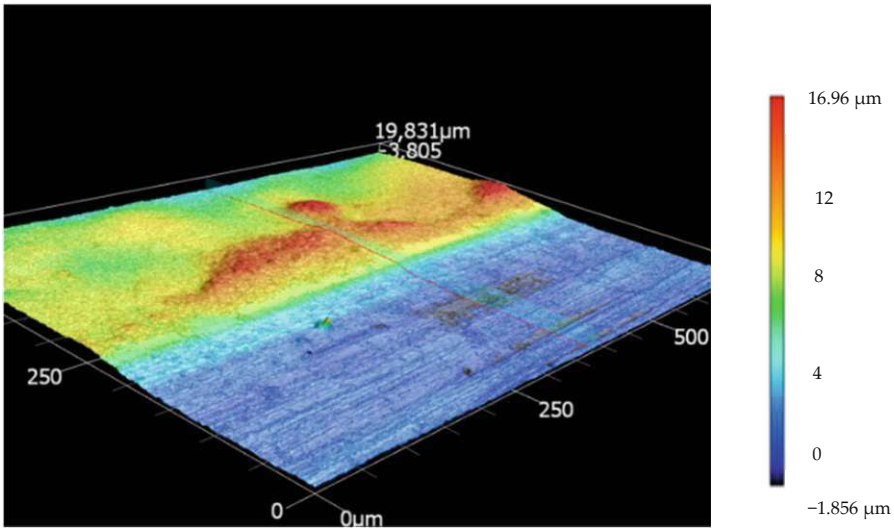


Figure 3. NF270 3D image. 20× measured by 3D laser-scanning microscope.

The water flux is higher and quick when the membrane is thin. In contrast, when a membrane is thick, the water flux is lower and slow due to the nanochannels being larger [33]. The thickness of the membrane for NF270 is 7 to 14 nm [34]. For that reason, the water flux is high due to the NF270 being a thin membrane.

3.2. Conductivity

The conductivity was measured in the permeate and the retentate vs. time, to evaluate the performance for lactic acid permeability in each membrane. The conductivity helps as a quick test to determine if there is a migration of ions from the feed tank to the permeate through the membrane. The conductivity was measured with a WTW TetraCon 925 conductivity probe coupled to a WTW Multi 3430. Samples from the retentate and the permeate were taken every 10 min. The measurements of the conductivity are shown in Figure 4, where the curves with the shapes filled in black represent the retentate, and the unfilled shapes represent the permeate.

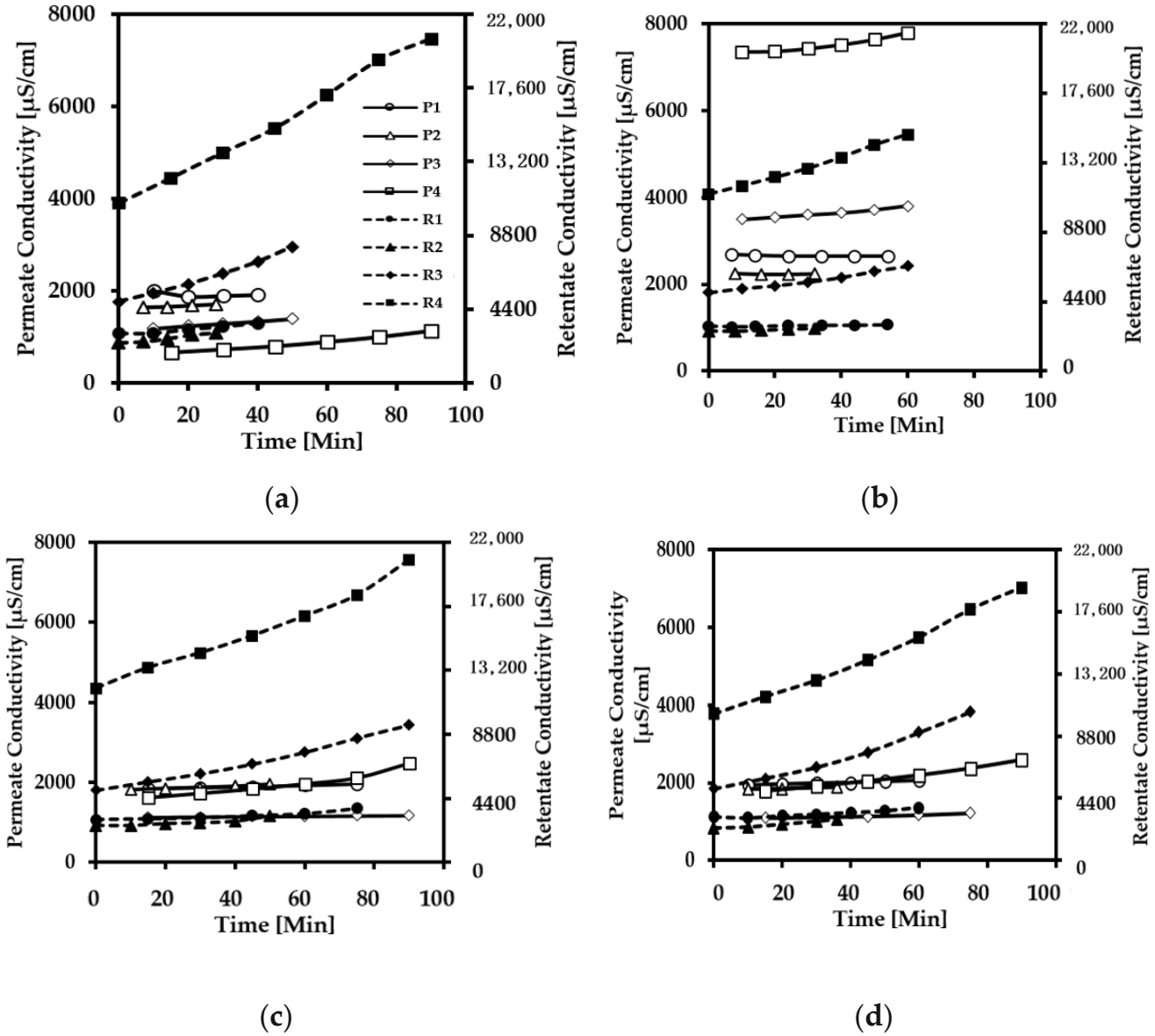


Figure 4. The conductivity of the lactic acid solution thought different membranes: (**a**) NF270, (**b**) SelRO® MPF-36, (**c**) Toray NF, and (**d**) Alfa Laval NF. P1 and R1, P2 and R2, P3 and R3, and P4 and R4 belong to experiments 1, 2, 3, and 4 listed in Table 3. P is permeate and R is retentate.

The pH adjustment influenced the conductivity of the retentate directly in all of the tested membranes. The conductivity in the retentate increased by 21, 24, 85, and 91% compared to the feed (initial measurement) for experiments 1, 2, 3, and 4, respectively, using the membrane NF270 (Figure 4a). Experiment 4 for NF270 had a substantial increase in the conductivity of the retentate, from 10,370 to 19,300 µS/cm. This result can be attributed to the high pH adjusted by NaOH, which increases the presence of ions in the solution and increases the lactic acid dissociation. Moreover, the conductivity in the retentate for the SelRO® MPF-36 membrane increased by 4, 22, 33, and 34% for experiments 1, 2, 3, and 4, respectively, compared to the initial feed which is represented in Figure 4b. The slightly increasing retentate conductivity regarding experiments 3 and 4 in MPF-36 is due to the MWCO of 1000 g mol^{-1}; therefore, this characteristic allows NaOH and lactic acid to pass through the membrane. There was only a 1% difference in the conductivity between pH 3.9 and 6.0, and the lowest increment was in experiment 1. Regarding Toray NF (Figure 4c), the conductivity in the retentate increased by 26, 26, 74, and 91% for experiments 1, 2, 3, and 4, respectively, compared to the feed. This means that when Toray NF is used, the conductivity in the retentate at 25 °C and 40 °C increases in the same percentage at pH 2.8. Concerning the Alfa Laval membrane (Figure 4d), the conductivity in the retentate also increased compared to the feed solution by 21, 29, 100, and 86% for experiments 1, 2, 3, and 4, respectively. The Alfa Laval NF membrane showed a considerably high difference in experiment 3 in terms of the conductivity of the retentate being a double value compared to the initial feed, from 5000 to 10,000 µS/cm. In the four tested membranes, the conductivity in the permeate side was lower than in the retentate at pH 2.8. It suggests that lactic acid does not pass entirely to the permeate side.

The conductivity in the permeate and the retentate depends on the MWCO of the membrane and the charge. With a higher MWCO, the conductivity in the retentate stream is lower compared to the lowest MWCO of the membranes. This behaviour can be related to the sieving effect in the MPF-36 membrane regarding the pore size. In addition, the increase in pH is directly related to the conductivity increment because LA dissociates at a higher pH above 3.86.

3.3. pH Variation in the Permeate and Retentate

pH is a key factor that strongly influences the membrane and the electrolyte solution, specifically in weak acids [35], e.g., lactic acid. pH also affects the charge of the active and selective layers of membranes. The pH is measured with a WTW SenTix H pH electrode coupled to a WTW Multi 3430 pH meter, calibrated against standard buffers at pH 4.00, 7.00, and 10.00. Samples were taken every 10 min. The results of the measurements are presented in Figure 5. The curves with the shapes filled in black represent the retentate, and the curves with the unfilled shapes show the permeate.

After the membrane filtration of the lactic acid solution at pH 2.8, 3.9, and 6.0, the pH of the resulting retentate was 2.8, 4.1, and 6.1, respectively, for NF270 (Figure 5a). For the SelRO® MPF-36 membrane (Figure 5b), the initial pH was 2.8, 3.9, and 6.0, and the obtained pH of the retentate after the filtration process was 2.6, 3.8, and 6.0, respectively. For the MPF-36 membrane, the pH of the retentate was slightly lower than the initial pH at 2.8 and 3.9. For the Toray NF membrane (Figure 5c), the pH variation occurred for 2.8, which decreased by 7% in the retentate compared to the feed, for the pH 3.9 in the feed, the retentate increased by 6%, with a final pH of 4.1; it shows the same behaviour as NF270. The tight membrane with a MWCO of around 200–300 g mol^{-1} has a similar tendency in pH variation over time (Figure 5d). However, a loose membrane, such as MPF-36, with a MWCO of 1000 g mol^{-1}, shows no differences in the pH variation of both the permeate and the retentate over time.

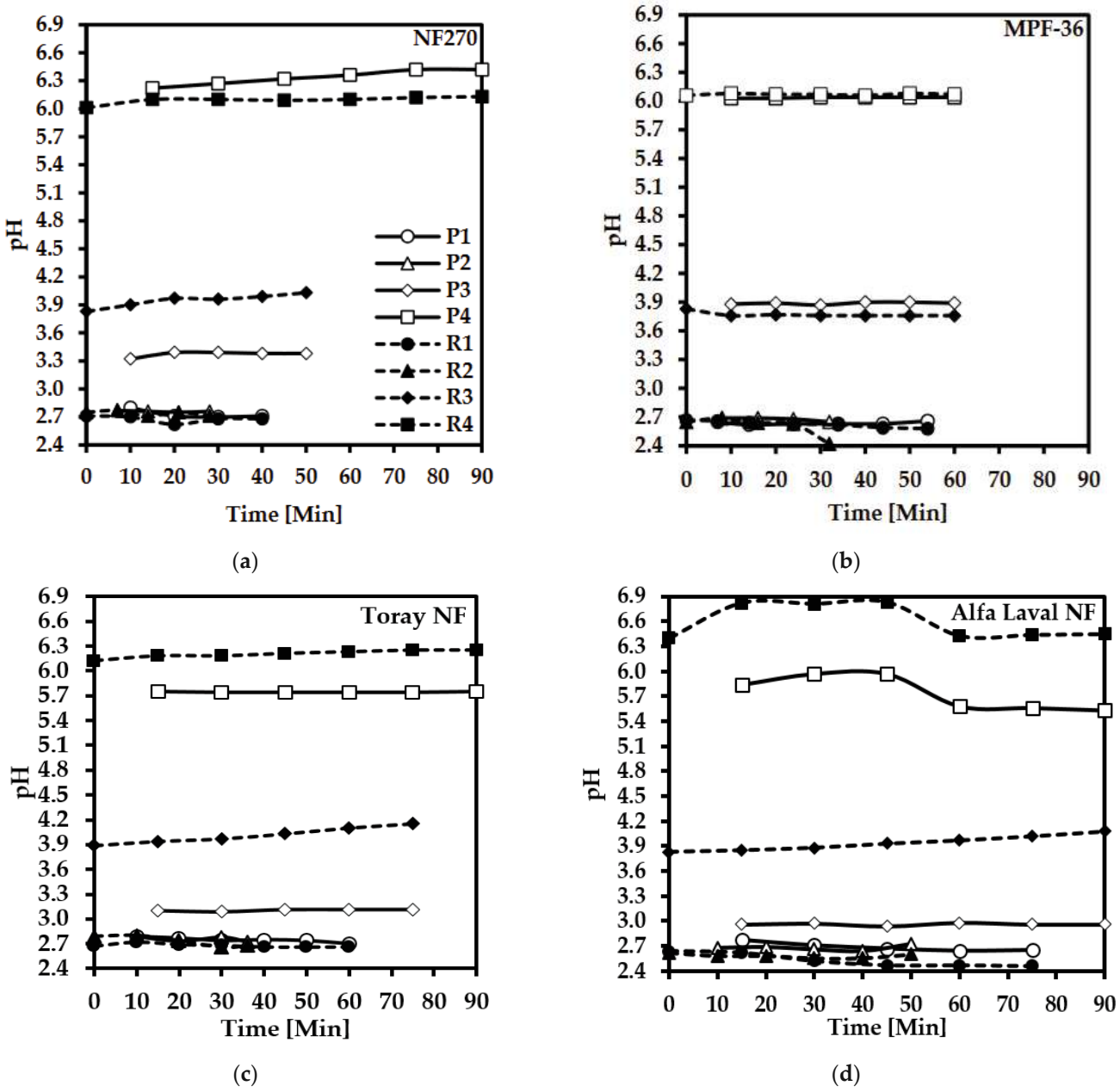


Figure 5. pH variation of the binary solution of lactic acid over time using different membranes: (**a**) NF270, (**b**) SelRO® MPF-36, (**c**) Toray NF, and (**d**) Alfa Laval NF. P is the permeate, R is the retentate, and the numbers indicate the experiments listed in Table 3.

3.4. Lactic Acid Permeability

The term permeability in this work refers to the accumulated amount of lactic acid in the permeate. The objective of the nanofiltration was to have low lactic acid rejection. This means lactic acid concentration must be low in the retentate, and the concentration of this compound should be high in the permeate.

3.4.1. Effect of the pH

The pH of the solution strongly influenced lactic acid permeability (Figure 6). The retention of LA increased with the pH increasing. At pH 3.9, the retention of LA was 73% for NF270, 24% for MPF-36, 80% for Toray NF, and 80% for Alfa Laval NF.

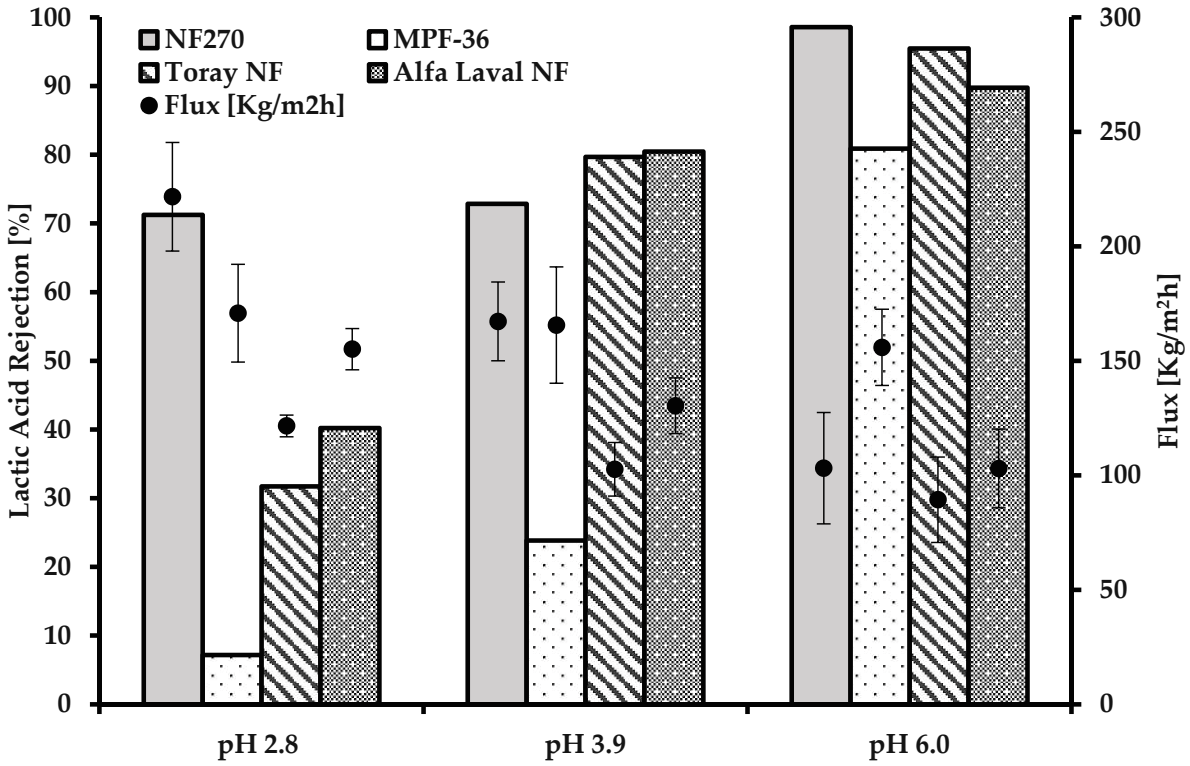


Figure 6. Rejection of lactic acid at different pH.

The lowest rejection of lactic acid was at pH 2.8. For NF270 this was 71%; for MPF-36 it was 7%, for Toray NF it was 32%, and for Alfa Laval NF it was 40%.

The lowest rejection of lactic acid contained in the binary solution was for the MPF-36 membrane at pH 2.8 and 25 °C reaching a 7%, Figure 6. Therefore, the permeability of LA was 93% in the permeate.

At a high pH (above 3.86), LA is dissociated in lactate ($C_3H_5O_3^-$) and proton (H^+) due to the pKa of the lactic acid. On the other hand, nanofiltration membranes have negatively or positively charged surfaces depending on the pH [36]. A membrane charged negatively will reject most lactate due to electrostatic repulsion, whereas a positively charged membrane will pass most lactate due to electrostatic attraction. The electrostatic interaction is produced in all commercial membranes due to an isoelectric point. The isoelectric point is the neutral charge of the membrane at a specific pH. The pH range for the isoelectric point among all the membranes varies depending on the composition.

Regarding the relationship between nanofiltration membranes and pH, if the solution pH is lower than the isoelectric point (IP), the membrane will be positively charged, and membranes will be negatively charged if the pH is higher than the IP. This modification of charges leads to changes in porosity and the membrane surface conformation. As a result, there is a reduction in the permeate flux.

In the case of experiments at pH 3.9 and 6.0, these are over the isoelectric point of each membrane; therefore, in every investigation, the membrane is negatively charged except for MPF-36, which was only negative at pH 6.0. It avoids lactate transport through the membranes, as lactic acid at a pH over 3.86 is dissociated, resulting in a high rejection of lactic acid. In addition, the increase in the pH of the LA solution leads to an increase in viscosity [14].

The dissociation constant of any compound is calculated by the Equation of Henderson–Hasselbalch [36]. The dissociation degree of lactic acid depends on the pH. The high yield could be obtained by changing the pH. pH 3.8 and 6.0 lead to more dissociated LA than lactate [24]. However, LA remains undissociated for the lower pH 2.8; therefore, the

permeability is higher. The dissociation of lactic acid at pH 2.7 is 6.47, at pH 3.9 is 48.14, and at pH 6.0 is 99.28%, respectively [37].

At a higher pH above 3.8, the dissociation of lactic acid increases and leads to increased rejection. Therefore, it is concluded by our experimental work that pH plays a role in the transport of lactic acid through nanofiltration membranes. Kumar et al., 2020, achieved 37% lactic acid rejection at pH 2.5 through partitioning methods [6]. These results agree with our research; at lower pH, the permeability of LA is higher. The pH of the permeate and the retentate of lactic acid transport through membranes is required to validate any mathematical simulation model.

On the other hand, the flux of the binary solution of lactic acid decreased markedly for NF270, Toray NF, and Alfa Laval when the pH increased. For NF270, MPF-36, Toray NF, and Alfa Laval at pH 2.8 compared to pH 6.0, the flux decreased in all the experiments by 53%, 8%, 26%, and 33%, respectively. In addition, there is a correlation between rejection and flux. At a high rejection of lactic acid, the flux was lower; therefore, the pH plays an important role with both parameters.

3.4.2. Effect of Temperature

At high temperatures, LA is dissociated in the solution [37], and the membranes allows sorption through them. The rejection of lactic acid is affected by increasing the temperature for the Toray NF and Alfa Laval NF membranes due to the Donnan effect, while for MPF-36, the Donnan and the sieving effect (Figure 7). In contrast, the rejection of lactic acid decreases at higher temperatures due to sorption for NF270.

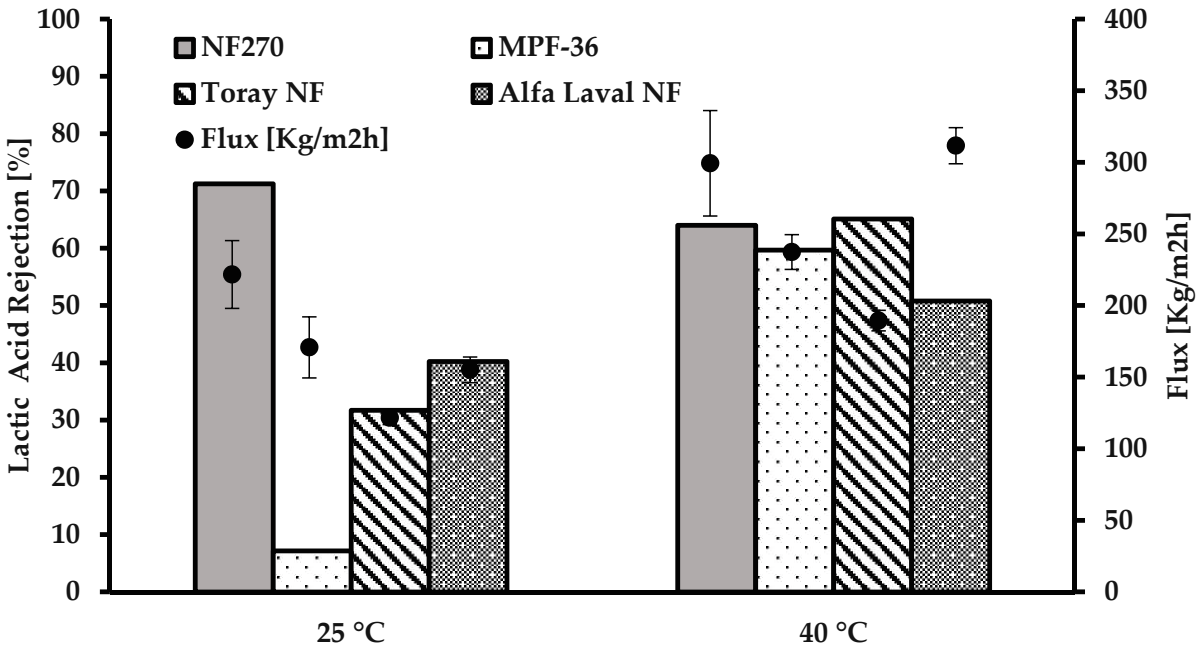


Figure 7. Rejection of lactic acid at different temperatures and flux variation.

The rejection of LA on the NF270 membrane decreased by 10% at 40 °C compared to 25 °C. On the other hand, lactic acid retention increased by 88, 51, and 21% for MPF-36, Toray NF, and Alfa Laval NF, respectively.

Temperature is one important operating parameter that improves the flux and affects the rejection of LA. LA retention increased by 88% for MPF-36, and the lowest rejection increase was 21% for Alfa Laval NF when the temperature was 40 °C in comparison with 25 °C. However, for NF270, the rejection of lactic acid decreased when the temperature increased.

The highest permeability yield (93%) for lactic acid was obtained when MPF-36 was used at 25 °C and pH 2.8. This yield is close to Novalin and Zweckmair, 2009 [38], with 89% of LA permeability.

Regarding the flux in the nanofiltration of the lactic acid binary solution, it increases when the temperature increases as well as the rejection. The flux increased by 34, 28, 35 and 50% for NF270, MPF-36, Toray NF, and Alfa Laval NF, respectively, when the temperature rises from 25 to 40 °C. The most affected membrane regarding the flux when the temperature increased was Alfa Laval due it reaches 50% of a higher flux.

4. Conclusions

Lactic acid is one of the leading products from grass silage juice; it has important uses in numerous industrial applications. The permeability of LA is an essential consideration in purifying LA when using the adequate membrane for downstream processing. Nanofiltration is used to study the transport of binary solutions (lactic acid and water).

The experiment showed that nanofiltration is useful for lactic acid separation but depends strongly on the characteristics of the membrane regarding the selective layer charge, the pore size, and the composition. MPF-36 presented the best performance for lactic acid permeance at 25 °C and pH 2.8, with a 93% yield; as MPF-36 is a loose membrane, the permeance is mainly due to its pore size characteristic. However, a poor performance was given by NF270 with an LA rejection of 71% at the same operating conditions. The optimal operating parameter for lactic acid transport was found at pH 2.8 and 25 °C in all four tested membranes.

On the other hand, when the pH increases, the flux decreases for the binary solution of lactic acid; in contrast, the flux increases as well when the temperature increases.

The pH variation of the feed directly influences the charge of the membrane due to the isoelectric point. Therefore, this parameter must be considered to recover certain compounds and their dissociation grades from obtaining a high permeability of lactic acid.

The experimental data of the pH and the conductivity in both the permeate and the retentate of the process will help select the optimal lactic acid permeability performance for further downstream processing and process scale-up.

Author Contributions: Conceptualization, M.C.-G. and A.A.; methodology, M.C.-G. and A.A.; validation, M.C.-G., A.A., K.M., M.S., C.J. and M.H.; formal analysis, M.C.-G., A.A., K.M. and M.S.; investigation, M.C.-G. and A.A.; resources, M.H.; data curation, A.A. and M.C.-G.; writing—original draft preparation, M.C.-G. and A.A.; writing—review and editing, M.C.-G., A.A. and C.J.; visualisation, A.A. and M.C.-G.; supervision, M.H.; project administration, M.H.; funding acquisition, M.H. All authors have read and agreed to the published version of the manuscript.

Funding: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 860477–AgRefine–H2020-MSCA-ITN-2019.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Thomas Jung for the chemical analysis.

Conflicts of Interest: The authors declare no conflict of interest.

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Perspective

Development of a Model for the Implementation of the Circular Economy in Desert Coastal Regions

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Abstract: Food production is the main challenge for developing arid regions due to the restricted access to fresh water. This study combines the environmental know-how of two coastal desert regions on the American continent with similar geographical characteristics to propose a general model for a circular economy in stressed environmental conditions. The Atacama Desert, located in Chile, is the driest place on Earth. Due to the lack of rainfall in decades, the possibility of growing food is almost impossible. The Desert of Sonora, in the northwest of Mexico, is known for its extreme aridity and temperatures over 50 °C in summer. Both deserts have continuously growing cities ranging from 400,000 to 900,000 inhabitants, where access to and management of freshwater represents an issue. A circular economy model was developed. Critical parameters for this model considered: the utilisation of solar energy for water desalination and energy production, integrated with hydroponic farming and water dosing with hydrogels for food production; microalgae for biofuels; seaweed for biochemicals; anaerobic digestion for organic waste management and nutrient recovery from wastewater sludge treatment. Regional policies and governance are needed to incentivise the adoption of circular economy models.

Keywords: circular economy; desertification; water scarcity

Citation: Cabrera-González, M.; Ramonet, F.; Harasek, M. Development of a Model for the Implementation of the Circular Economy in Desert Coastal Regions. *Land* **2022**, *11*, 1506. https://doi.org/10.3390/land11091506

Academic Editor: Luca Salvati

Received: 30 June 2022
Accepted: 5 September 2022
Published: 7 September 2022

1. Introduction

Water scarcity and desertification could affect up to 75% of the world's population by 2050. Due to climate change, the world needs to prepare for desertification and water scarcity, and the regions subject to drought and extreme weather conditions must lead the way.

A circular economy model focusing on maximising the efficient utilisation of water resources is needed to ensure the Sustainable Development Goals (SDGs) of good health and well-being (SDG 3), clean water and sanitation (SDG 6), zero hunger (SDG 2), sustainable cities and communities (SDG 11), responsible consumption and production (SDG 12), and climate action (SDG 13).

The restricted access to fresh water in desert regions represents a challenge in their food production. Integrating their food production systems with state-of-the-art nutrient recovery systems like anaerobic digestion can close the water and nutrient loops. Desert Coastal Regions (DCRs) have a unique environment with abundant seawater and solar radiation resources.

Water desalination is the main source of fresh water in DCRs. Minimising water desalinisation costs is one of the significant challenges for developing a circular economy in these regions. In addition, maximising freshwater usage for agricultural, commercial, industrial and residential use also represents a challenge.

The transition from a linear to a circular economy requires technology, sustainable processes, innovation, products and services [1] that all have to be developed wisely between stakeholders (private sector, government, and citizens), integrating public policies

and laws. On this transition, water-management utilities are crucial to push the water sector into a more sustainable development [2].

However, a circular economy model cannot be universal; it depends on the climate conditions, biodiversity, and geographical location, and the implementation will be laid on government policies.

2. Environmental Characteristics of the Atacama Desert, Chile, and Sonoran Desert, Mexico

The Atacama Desert (AD) is the driest non-polar and oldest (since the Jurassic period to Miocene, 5,000,000 years ago) desert on Earth [3]. The AD is located on the western coast of central South America, beside the Pacific Ocean, from the north of Peru (5° S), ending close to La Serena, Chile (30° S) [4]. The AD's main characteristics are toxic elements, strong oxidising conditions, extreme aridity, high ultraviolet radiation levels, and low-to-zero concentration of soil carbon [3]. Additionally, precipitation in the AD is scarce (20 to 80 mm per year) and is intensely concentrated in the summer [5], with January and February being the two "rainiest" months. Due to this low level of rainfall, there is almost a complete absence of vegetation [6].

The average annual temperature is 16.1 °C, with a maximum temperature of 36 °C and minimum of −3.79 °C [4]. The hyper-arid climate is controlled by the upwelling cold Humboldt current in the Southeast Pacific Ocean and the high-pressure belt generated by the global Hadley circulation [7]. In addition, the AD, specifically the Antofagasta region, hosts Chile's major extractive mining economy. Antofagasta represents 51% of the mining Gross Domestic Product (GDP), and 26% of the world production of lithium comes entirely from the Atacama Salt Lake [8].

On the other hand, the Sonoran Desert (SD) is located between 23° N and 33° N in North America including the states of Sinaloa and Sonora, and the Peninsula of Baja California [9]. The SD covers an area of 260,000 km^2 [10]. This region is surrounded by the Gulf of California and the Pacific Ocean and has less than 50 mm of rainfall per annum; however, Sonora's plain can receive up to 250 mm [10]. The temperature within the SD drops to −5 °C in winter, while in summer it can be up to 50 °C. The SD is one of the hottest deserts on Earth [11].

3. Circular Economy Model

The Circular Economy (CE) is a paradigm changer of the current linear production systems. In order to achieve major breakthroughs, leveraging slight shifts in perspectives is needed [12].

The CE concept was first introduced by Pearce and Turner [13] explaining the interdependence between the environment and the economy in their book. Among the different CE definitions, the following two exemplify its context.

The CE can be defined as "an economic system that replaces the 'end-of-life' concept with reducing, reusing, recycling, and recovering materials in production, distribution, and consumption processes" [14].

The Ellen Macarthur Foundation [15] defines the CE as "a new economic model that is restorative or regenerative by design and focuses on resource-related challenges for economies and businesses". In the CE, the life cycle must be well planned to eliminate waste by utilising it as a feedstock or recirculating it.

CE can be successfully implemented as a management model to achieve sustainable development. This management model can be used for establishing and executing regulations to protect the environment; establishing a system of preferences for circularly managing resources; promoting cooperation between stakeholders to achieve a collaborative sharing economy; and strengthening the social capital [16]. Studies from Neves and Marques [17] have shown the drivers and barriers to transition from a linear to a circular economy, evaluating the role of social, environmental, and economic factors. The authors recommend that, in order to achieve an effective transition to a CE, promoting

policies targeting specifically older and less-educated people is needed, due to the lack of environmental awareness of these groups. Smol, Adam, and Preisner [18] proposed a circular economy model for the water and wastewater sector focusing on the circular economy principles of reduction, reclamation, reuse, recycling, recovery, and rethink. They found that the sustainable management of water resources is not sufficient to achieve the CE objectives and that a special emphasis is needed on wastewater disposal.

Furthermore, Mannina et al. [2] reviewed the water and sewage sludge policies in Europe and analysed the barriers, bottlenecks, opportunities and challenges of applying the CE in the wastewater sector. The authors concluded that the barriers should be considered as challenges to guide policymakers and water-management utilities to resource recovery decisions.

According to Ferronato et al. [19], circular economy models vary in every context due to social, environmental, financial, and political differences; hence, they cannot be equivalent for every context. The authors emphasize that the implementation of a CE model should consider applying specific plans depending on the needs of the country, state, city or community.

On the other hand, Ahmed, Mahmud, and Acet [20] exposed that circular economy models are usually applied in developed countries but rarely in developing ones. In their scientific research, they mentioned that the major practices for a CE in North America (United States) are making homes using old containers, making carpets out of plastic, recycling and reusing used clothes and making jeans from waste plastic bottles; while in South America (Chile), the focus is on recycling and reutilisation of wastewater, and recycling of solid wastes.

Research on desert areas for a circular economy is rare. For this reason, this study focused on a macroscale model for DCRs.

This study proposes a circular economy model integrating state-of-the-art technologies with the two most abundant natural resources in DCRs: solar radiation and seawater. Solar energy can be harvested from solar panels to provide electricity to a desalination plant.

A circular economy in DCRs can be possible if all the natural resources are used sensibly. One such resource is the availability of seawater next to the desert, which poses an advantage in fighting water scarcity with a desalination process to supply the water requirements fully or partially for inhabitants, food production, and industrial processes.

Another advantage of desert areas is the high solar radiation, which can be used to produce energy through solar panels.

Furthermore, clean energy production is possible in deserts, and it will fulfil the requirements for water desalination. An additional advantage is the availability of non-arable land that can be utilised for microalgae cultivation in open raceway ponds or photobioreactors. An alternative for non-arable land farming for fresh food production is hydroponic systems. Moreover, seaweed cultivation for food production is also possible.

An example of technology integration was set by Bermudez-Contreras et al. [21], who designed a reverse osmosis desalination plant powered with photovoltaics for the State of Baja California Sur. To produce 1 m^3 of potable water, including pre-treatment and post-treatment processes, 3.5–4.5 kWh are needed [22]. The energy demand of the desalination plant can be satisfactorily filled with solar energy (see Section 3.2).

The desalination process has the disadvantage of producing a sidestream: brine. Brine's main constituents are the salts removed by reverse osmosis, which are discarded in the seawater. Therefore, brine is a potential contaminant and is a candidate for environmental damage that must be mitigated since sustainability is key in a CE process. However, brine can be converted or recovered into new products (ions or molecules) like MgO, Rubidium, Uranium, NaOH, Cl_2, H_2, acids, bases, Lithium, and salts in pure form [23] to avoid environmental impact. High solar radiation in arid regions can be an excellent ally for evaporating the brine in a closed and controlled environment. The evaporation process can be helpful for mineral and nutrient recovery like phosphate, which could be applied in hydroponics as a fertiliser (see Section 3.3).

For the model proposed, once the water has been desalinated, the freshwater is utilised for hydroponic farming in the case of non-arable soil (e.g. Antofagasta) or it can be used for irrigation water dosing with hydrogels in the case of semi-arable soil (agricultural land in Sonora). Seawater can be utilised for microalgae production in raceway pounds, and seaweed can be farmed in the ocean. Seaweed is utilised for biochemical production, while microalgae are used for biofuels production, among other applications.

Then, the residue streams from the agricultural systems, microalgae and seaweed can be processed through anaerobic digestion for biogas production. Nutrients can be recovered from the digestate, while biogas is upgraded into biomethane, utilising CO_2 as feed for the microalgae. A combined heat and power unit can also be employed to produce electrical energy for the grid and heat for the desalination process, capturing the exhaust gas, purifying it, and feeding the CO_2 to the microalgae. The digestate can be directly applied in agriculture, or the recovered nutrients can be added to the hydroponic system. Byproducts, such as glycerol from biofuel production, improve biogas yields in anaerobic digestion.

The details discussed above can be visualized in Figure 1, which details a schematic of a circular economy model that could be implemented in coastal arid regions.

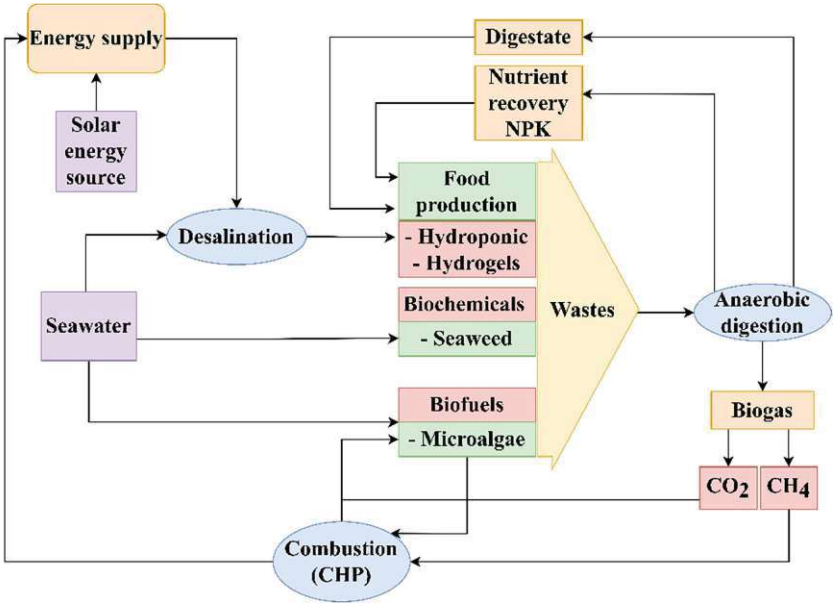

Figure 1. Schematic of a suggested circular economy to develop in coastal arid regions.

This model represents a macro scale system of a CE and does not consider other factors like industries, pollution, tax policies, environmental laws, etc. Nevertheless, this model can be considered as a starting point for implementing an action plan for the social economy in Chile, Mexico or Latin America, as the European Commission suggested [24].

The fundamental principle of the proposed model is integrating state-of-the-art technology with abundant natural resources, i.e., ocean water and solar radiation, exploited through renewable energy and responsible reintegration of treated brine into ocean waters. In summary, this paper proposes the use of desalinated water for food production using a hydroponic or irrigation system that doses water with hydrogels. Whereas, seawater will be utilised for macroalgae and microalgae farming to produce biochemical and biofuels. Crop and algae residues will be processed through anaerobic digestion to obtain biogas and digestate, where the biogas will be upgraded, and the carbon dioxide stream is fed to the microalgae. Nutrients will be recovered from the digestate and used for food production. Alternatively, the biogas can be burnt in a combined heat and power unit to produce electrical and thermal energy, from which the resultant CO_2 can be fed to the microalgae.

In the following section, the subsystems of the model and their current state in the Atacama and Sonoran deserts are described.

3.1. Water Desalination

Water scarcity in desert places is a challenge for the inhabitants of the regions. The World Resources Institute has ranked Chile as number one and Mexico seventh in having a high baseline water stress [25]. Nevertheless, AD and SD have the advantage that they are next to the Pacific Ocean; therefore, water desalination plants play an essential role in freshwater conversion. Water desalination (WD) can be achieved by reverse osmosis with membranes or thermal energy. In reverse osmosis desalination, membranes remove all the salts and unwanted particles to convert seawater into drinking water (Figure 2). However, WD is a costly, energy-intensive and non-environmentally friendly process. In South America, Chile has the most extensive system of desalination plants [26]. The oldest desalination plant started operations in 2003 in Antofagasta (Figure 3A). The plant supplies 85% of the Antofagasta population with potable water, making it the biggest desalination plant in Latin America. In total, in Antofagasta, it is produced 73,440 m^3 of desalinated water per day [27].

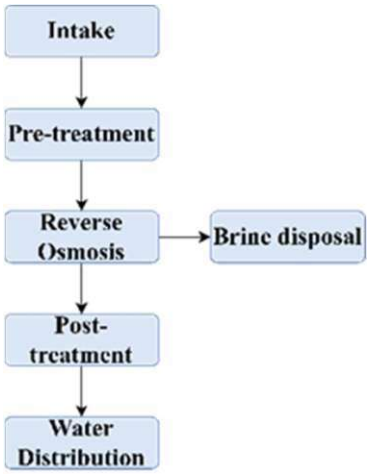

Figure 2. Flow diagram of water desalination.

Chile discards the brine by pumping it back into the ocean; however, other countries utilise other disposal methods, such as evaporation ponds, deep-well injection, conventional crystallisers and discharge to the sewage system [28].

(**A**) (**B**)

Figure 3. (**A**) Desalination plant in Antofagasta, Chile [29]. (**B**) Desalination plant in Guaymas, Sonora, Mexico [30].

Mexico has over 435 desalination plants, of which 71 are in the state of Baja California Sur [31], part of the Sonoran Desert. In the case of Sonora State, in 2008, three desalination plants were approved with varying capacities of 200 L s^{-1} for Guaymas (Figure 3B) and Hermosillo, and 120 L s^{-1} for Puerto Peñasco [32]. Robles-Lizárraga et al. [33] designed an optimal desalination plant for the city of Puerto Peñasco in Sonora. The 200 L s^{-1} (720 m^3 h^{-1}) desalination plant in Guaymas started operations this year to provide fresh water to its city [34].

The ambitious binational water desalination opportunities report for the Sea of Cortez aims to find the most optimal sites to install desalination plants to provide fresh water to the states of Sonora and Baja California Norte in Mexico and Arizona, Nevada and a small part of California in the United States of America [35].

3.2. Solar Energy

Globally, the Atacama Desert in Chile is one of the best places for astronomy due to its lack of clouds and possesses one of the most significant solar resources. Additionally, global irradiation in the AD is above 2500 kWh m^{-2} $year^{-1}$, making it the place with the highest radiation level on the planet [36]. This solar potential means that the production of energy through solar panels is possible. Currently, nine of the ten biggest solar plants in Chile are in the AD (El Romero, Solar Bolero (Figure 4), Luz del Norte, Finis Terrae, Cornejo Solar, Amanecer CAP, El Pelícano, Carrera Pinto, and Pampa Solar Norte). Antofagasta has one of South America's biggest solar power plants, producing 439.1 GWh [37].

Figure 4. Bolero Photovoltaic Park, Sierra Gorda, Antofagasta, Chile [38].

In the state of Sonora, the eighth biggest solar plant in the world, comprised of 240 hectares, is currently under construction, which will harvest 1000 MWh [39]. If just 1% of Sonora's land was used for solar projects, it could provide enough energy to power all of Mexico [40].

3.3. Hydroponic Systems for Food Production

Hydroponic systems are soilless agricultural systems that grow plants in water with mineral nutrients. Hydroponics have many advantages compared to traditional agriculture due to limited water consumption, a limited need for pesticides, and a lack of arable use. Additionally, the system is completely controlled in terms of nutrient supply, temperature, light, humidity, and carbon dioxide concentration [41]. In desert regions, it is advantageous

to apply these techniques since there is a lack of fertile soils for agriculture combined with a limited freshwater supply.

In Antofagasta, Chile, specifically in the "La Chimba" and "Altos la Portada" zones, hydroponic cultures have been developed to supply a fraction of the food requirement for the population. The main products available through this type of agriculture are lettuces, spinach, coriander, parsley, bell pepper (Figure 5), chard, basil and others. These vegetables are sold in the city farmer's market "La Vega Central", as well as in supermarkets, and on the internet. The hydroponic system is supplied by desalinated water, making it the most extensive hydroponic production in Chile.

Figure 5. Hydroponic system of bell peppers, Alto la Portada, Antofagasta, Chile.

Before the hydroponic system was set up in Antofagasta (2012), all the fresh vegetables came from Arica or La Serena (the vegetables produced at present by hydroponics). Terrestrial transport was needed due to the long distances to fertile soils (La Serena to Antofagasta: 865 km; or Arica to Antofagasta: 716 km) to provide fresh food to consumers.

In the case of Mexico, Rafael Martinez-Cordova et al. [42] evaluated an integrated multitrophic aquaculture system that utilised fish aquaculture of *Tilapia* spp. and the agriculture of jalapeño and mini bell peppers in greenhouses in Hermosillo. However, they found that jalapeño pepper plants were not an adequate candidate for hydroponics in the proposed system. De Anda and Shear [43] stated that vertical hydroponic agriculture could help resolve the food shortage caused by non-arable land and water scarcity. Shrivastava et al. [44] proposed a vertical automated hydroponic system that monitors the water flow, temperature, moisture and nutrients present in the water, while also recycling the utilised water. The authors developed a vertical hydroponic system that can reduce water consumption by up to 70%.

In Mexico in 2010, 60% of the installed hydroponic greenhouses failed due to the absence of qualified technicians, lack of producer training, and inadequate location of markets [45]. However, by 2014, more than 20,000 ha were working with hydroponics [46].

3.4. Water Dosing with Hydrogels for Agriculture

According to the World Economic Forum [47], agricultural production systems need to increase their productivity by two-thirds to meet the projected demand in 2030 caused by the population increase. The implementation of more water-efficient systems is needed to meet this demand.

Hydrogels are yield enhancers and soil conditioners, which can retain nutrients and water, and then release them over an extended period [48]. Kalhapure et al. [49] found that applying hydrogels increases productivity in terms of crop yield.

The emergence of hydrophilic polymers based on polyacrylamide occurred in the 1950s in the United States of America. Over the years, its hydration capacity has improved from 20 to 400 times its weight [50].

Hydrophilic polymers help improve the water absorption capacity, allowing to improve the efficiency of water use, the effect of which depends on the quality of the water, with the hydration capacity of the polymer being significantly reduced in the presence of salts in the irrigation water [51].

The combination of superabsorbent hydrogels and fertiliser produces slow-release fertiliser hydrogels, improves plant nutrition, and reduces the environmental impact of conventional fertilisers since there are fewer losses by evaporation and the irrigation frequency is reduced [52].

López-Elías et al. [51] implemented hydrogels for the greenhouse production of Anaheim peppers. They found that this initiative favours the reduction of the volume of water applied and the frequency of irrigation, favouring the increase in chlorophyll content without affecting the crop.

Macías-Duarte et al. [53] performed a study on the integration of hydrogels with irrigation systems for the cultivation of olives. They found that, with an irrigation deficit of 50%, the yields and quality of olive trees were not affected, nor was the soil's moisture content.

3.5. Microalgae Culture as a Biomass and Seaweed Farming and Processing for Food Supply and Biochemicals

Microalgal biomass represents an attractive feedstock for producing human protein supplements, liquid fuel, feed for the aquaculture industry, biofuels and CO_2 capture. In addition, microalgae produce high-value byproducts like pigments, enzymes, lipids, sugars, sterols and vitamins [54]. The advantages of microalgal biomass production are that they can be grown using wastewater, seawater, brackish water, and sunlight, and there is no need for arable lands [55]. Consequently, AD and SD have the potential for microalgae production due to the proximity to the ocean, sunlight, and the availability of non-arable soils, making an ideal scenario for biomass production. Rasheed et al. [56] described the possibilities of cultivating microalgae in Qatar, which is located next to the Persian Gulf. The climate conditions of Qatar improved the microalgae's nutritional potential in terms of lipids, polyunsaturated fatty acids, and proteins.

Furthermore, Schipper et al. [57] have demonstrated four novel isolated microalgae strains from the Arabian Gulf. Their results suggested that *Picochlorum* sp. can grow in elevated temperatures (40 °C) and high carbon dioxide concentrations, making them promising organisms for CO_2 sequestration. Regarding biofuels, Gao et al. [58] successfully improved *Chlorella* sp. cultures using a mixture of seawater and domestic sewage for biofuel production, obtaining the highest productivity of lipid when 60% seawater was used. On the other hand, more than 70 different local microalgae species have been characterised and isolated in Mexico. However, only a small fraction of them has been explored for producing valuable products [59]. In Chile, some attempts to investigate phycoremediation using *Muriellopsis* sp. in the AD at a pilot-scale level have been done [60].

In the scientific literature, many applications and benefits of microalgae have been described; hence, microalgae production could be implemented in the CE model for DCRs due to their intrinsic value and low water demand.

Regarding macroalgae production, high-interest compounds have been identified for potential applications. Namely, fatty acids, phenols, pigments, polysaccharides and monosaccharides are target compounds obtained from seaweed [61].

The seaweed industry is most developed in Asian countries where most of the seaweed is cultivated with smaller amounts harvested or obtained from the wild. While in Europe, most of the seaweed industry utilises imported algae or is obtained from wild harvesting [62]. In the case of Latin America, Chile contributes 88% of the total seaweed harvested, while Mexico only contributes 3.7% [63].

According to the project AlgaHealth [64], ocean farming in the desert is needed to supply all the required dietary supplements. However, a lack of research on this topic has been found.

3.6. Biogas Production

The popularity of biogas production for energy production and waste neutralisation has been increasing worldwide since the early 2000s. Biogas is composed of the following concentrations: 60–70% methane, 30–40% carbon dioxide, 1–2% nitrogen, 1000–3000 ppm hydrogen-sulfide and 10–30 ppm ammonia [65]. Biogas is obtained by a process called anaerobic digestion.

Anaerobic digestion or degradation is a biological process that converts organic carbon by subsequent reductions and oxidations to its most reduced state (CH_4) and its most oxidised state (CO_2) in the absence of oxygen [65]. Biogas main applications are in the area of treatment of sludge from wastewater, Organic Fraction of Municipal Solid Waste (OFMSW), manures, agricultural and industrial residues [66].

In the case of Mexico, the federal government has expressed its interest to develop Wastewater Treatment Plants (WWTP) integrated with anaerobic digestion to produce and use their own energy to decrease operational costs [67]. An example of this is the WWTP of Hermosillo, which has two 12,000 m^3 anaerobic digesters, three combined heat and power units of 874 kW (two in operation and one on stand-by) and two gas holders of 2150 m^3 [68].

Kim, Lee, and An [69] proposed retrofitting the biogas plant of Hermosillo's main WWTP for co-digestion with the OFMSW, to generate electricity and heat for the WWTP. Whereas, Noyola et al. [70] carried out three pre-feasibility studies for anaerobic digestion in pig farms in Sonora; an up flow anaerobic sludge blanket at NORSON slaughterhouse and co-digestion of industrial residues at the WWTP of Hermosillo.

Mexico has no legislative framework allowing the utilisation of digestate from pig slurry for agricultural purposes [70]. Currently, there are no anaerobic digestion plants operating with manure or OFMSW on the AD or on the SD.

3.7. Nutrient Recovery from Wastewater Treatment Streams and Anaerobic Digestion

The increase in agricultural practices has led to the generation of a large amount of nutrient-rich wastewater [71]. Even though several reports address nutrient recovery technologies and the challenges of nutrient recovery from different nutrient-rich wastewaters, there is no standardised methodology to assess the feasibility of real-life applications [71].

Domestic wastewater treatment is a mature technology that impacts human health and the environment [72]. The two main alternative domestic wastewater treatment processes that recover energy and nutrients are low energy mainline for phosphorus recovery and partition–release–recover for nitrogen and potassium recovery [72].

Nutrient recovery technologies can be divided into low energy and high energy consumption. Struvite formation and ammonia stripping are two easily operated technologies that, when compared to membrane technologies, can be implemented at a low energy cost [73]. Membrane distillation, electrodialysis, reverse osmosis, and nanofiltration

are effective nutrient recovery technologies, but their long-term operation is limited by membrane fouling [73].

A particular case of nutrient recovery is planned for the WWTP in Marineo (Italy), where phosphorus and nitrogen will be recovered from the effluent streams by means of two adsorption columns [2]. In the state of Sonora, there are examples of utilising natural resources efficiently, such as the solar-powered wastewater treatment plant (Figure 6) serving the city of Nogales with a 220 litres of sewage per second installed capacity [74].

Figure 6. Solar-powered wastewater treatment plant in Nogales, Mexico [75].

Since the 1990s, the General Law of Ecologic Equilibrium and Protection of the Environment has pushed for wastewater treatment in Mexico. Article 92 of this law (when translated) states that "to ensure the availability of water and lower the levels of waste, the competent authorities will promote the saving and efficient use of water, the treatment of wastewater and its reuse" [76].

Due to water scarcity in Hermosillo, companies, schools, residential complexes, hotels and the airport have private wastewater treatment plants summing to 44 [77]. The two main government-owned WWTP in Hermosillo have a capacity of 2500 L s^{-1} (Figure 7) and 113 L s^{-1}, respectively.

Figure 7. The wastewater treatment plant in Hermosillo, Sonora, Mexico [78].

Water scarcity in DCRs can be decreased by implementing mature, proven technologies as the ones described above. Figure 8 shows the process followed in this perspectives article.

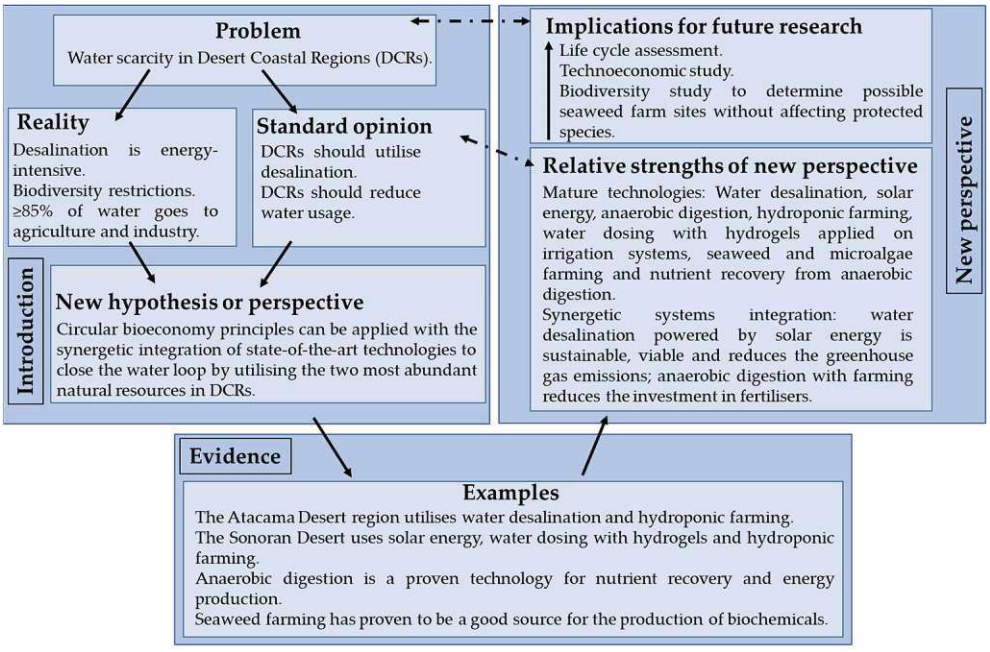

Figure 8. Scheme of the process followed in the article.

4. System's Feasibility and Evaluation

According to Corvellec, Stowell, and Johansson [79], a circular economy model needs to be accountable for its achievements and shortcomings; hence, the feasibility of implementing the proposed technologies needs to be addressed regarding the environmental risks, ecological sustainability, the economic viability and the technology readiness level.

To evaluate the proposed circular economy model, attributes were evaluated for the processes and products. The products and processes were evaluated from 0 to 10, with zero being poor performance and ten being outstanding performance. The four evaluated attributes are technology readiness level, economic viability, ecological sustainability, and

environmental risks. The technology readiness level assesses if the technology is ready for deployment; ecological sustainability evaluates the environmental effects; environmental risks refer to the irreversible environmental damage that could be done if the products or processes are not managed correctly; and economic viability evaluates the capital costs. Figure 9 shows the results of the evaluated attributes of the proposed circular economy model.

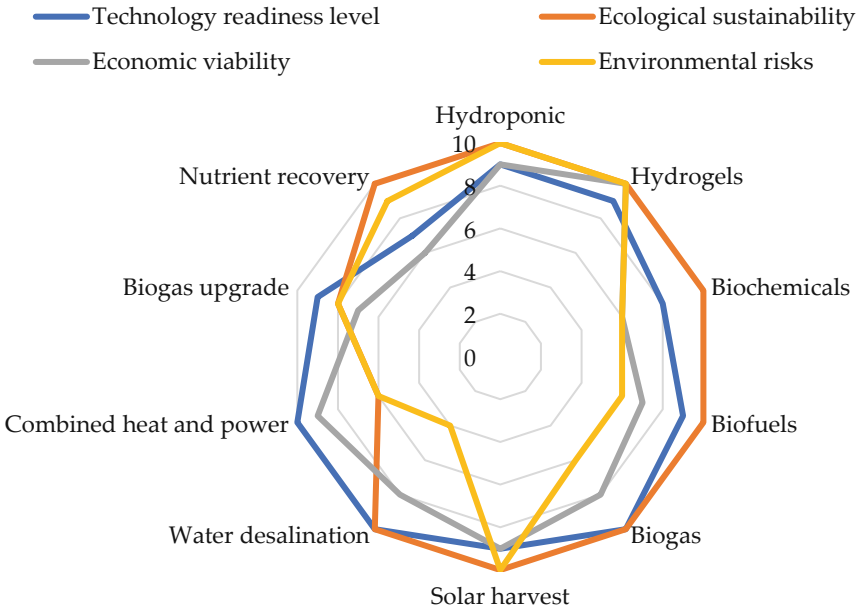

Figure 9. Attributes evaluation of processes and products of proposed circular economy model.

Out of the evaluated processes in Figure 9, the environmental risks are present in most of them except on solar energy harvesting, hydroponic system and water dosing with hydrogels. The worst performance for the ecological sustainability attribute is combined heat and power cogeneration, since there is an energy loss from 24% to 45% in the power generation [80]. Most of the processes analysed are mature, hence the technology readiness level is high. There is economic viability in most cases, being the lowest performance nutrient recovery.

A detailed evaluation is needed before deploying the proposed circular economy model for DCRs. To successfully integrate these technologies, feasibility can be assessed by a life cycle assessment, a techno-economic analysis, and a biodiversity study.

Finally, regional policies and governance must be available to incentivize the adoption of CE models.

The closest policy initiatives related to a CE in Chile are found in law No. 20,920 [81], residues management and recycling campaigns. However, it does not mention a circular economy per se. Nevertheless, the new Chilean constitution proposal mentioned that the state would promote the circular economy but did not explain how [82]. The priority products for recycling mentioned in article 10 of the Chilean law are lubricant oils, batteries, electric and electronic devices, containers and packaging, and tires.

The Ministry of Environment of Chile, as well as the Ministry of Economy, Development and Tourism of Chile, the Chilean Economic Development Agency (CORFO) and the Sustainability and Climate Change Agency, have made efforts to implement a Chilean circular economy by 2040 [83]. Seven goals are set to carry out a circular economy in Chile by 2040, in the following order according to priority (Ministerio de Medio Ambiente 2020): to increase green employment, decrease the municipal solid waste by inhabitants and the total waste generation by GDP, to increase the resource productivity, the general recycling rate and the recycling of municipal solid waste, and to recover sites affected by illegal waste disposal (Figure 10).

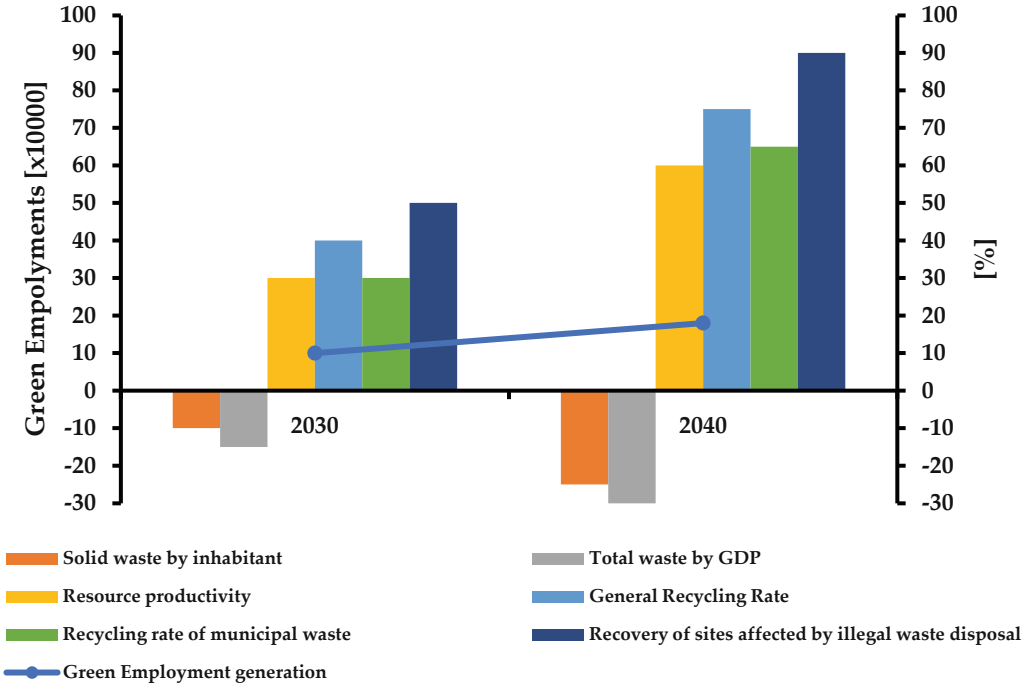

Figure 10. Long-term goals in Chile to implement a circular economy, adapted from [83].

In the case of Mexico, in November 2021, the General Law of Circular Economy was approved [84]. The law aims to establish the principles of the circular economy through legislation on waste and contribute to the fight against climate change and protecting the marine environment. Valenzuela-Corral and Hinojosa-Rodriguez [85] studied the implementation of the circular economy in the south of Sonora, considering the ecological, political, social, and technological factors. The authors concluded that, to implement the circular economy in this region, companies and governments must collaborate, innovate and have a vision of change. Cansino-Loeza et al. [86] proposed a framework for developing a model that provides the optimal allocation, quantifies, and maximises the security of the water, energy, and food sectors in the state of Sonora.

International organisations, governments, investors, and businesses must work together for this model implementation. International organisations can put the circular economy on the global climate agenda, governments can enable policies and put the necessary infrastructure in place, investors are needed to mobilise capital towards circular economy solutions, and businesses can make intelligent decisions on how to design and sell their products and services [87].

5. Conclusions

A circular economy model for the development of coastal desert regions has been proposed complementing the conditions and experiences of the Atacama Desert and the Sonoran Desert.

As reviewed in this paper, integrating desalination and hydroponic farming, solar energy and wastewater treatment, wastewater treatment and biogas production, and hydrogels and irrigation are already a reality in the Atacama Desert and the Sonoran Desert. Macroalgae offshore farming, microalgae production and nutrient recovery are the missing components needed for the implementation of the proposed model.

Studies are needed to ensure environmental, social, and economic sustainability before deploying pilot testing. Within these studies, life cycle assessment, techno-economic analysis, and a biodiversity study are recommended to ensure the deployment of this model without harming the environment or protected species.

Author Contributions: Conceptualization, F.R. and M.C.-G.; methodology, F.R. and M.C.-G.; validation, F.R. and M.C.-G.; formal analysis, F.R. and M.C.-G.; investigation, F.R. and M.C.-G.; resources, M.H.; writing—original draft preparation, F.R. and M.C.-G.; writing—review and editing, F.R. and M.C.-G.; visualisation, F.R. and M.C.-G.; supervision, M.H.; project administration, M.H.; funding acquisition, M.H. All authors have read and agreed to the published version of the manuscript.

Funding: This project has received funding from the European Union's Horizon 2020 research and innovation programme AgRefine under the Marie Skłodowska-Curie grant agreement No 860477.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors would like to express their great appreciation to the AgRefine colleagues Priya Pollard, Charlene Vance, and Mariana Cerca for proofreading the manuscript for English language correctness.

Conflicts of Interest: The authors declare no conflict of interest.

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Journal of Environmental Chemical Engineering 11 (2023) 110881

Contents lists available at ScienceDirect

Journal of Environmental Chemical Engineering

journal homepage: www.elsevier.com/locate/jece

Separation of lactic acid from fermented residual resources using membrane technology

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ARTICLE INFO

Editor: Dr Y Liu

Keywords:
Lactic acid
Organic waste
Microfiltration
Nanofiltration
Electrodialysis

ABSTRACT

Lactic acid can be derived from microbial fermentation and be used as a platform chemical in various industrial applications. This study aims to investigate the challenges involved in combining a low-cost, heterogeneous feedstock, such as a mixture of candy-waste and digestate, with an optimized downstream strategy to achieve maximum recovery of high-purity lactic acid, targeting low energy consumption. To achieve this goal, four membrane separation technologies, namely microfiltration, nanofiltration, monopolar, and bipolar electrodialysis, were combined to design two purification processes. Microfiltration served as the pre-purification step, followed by either process A, which combined nanofiltration and bipolar electrodialysis, or process B, a combination of monopolar and bipolar electrodialysis. The findings emphasized the importance of pH as a control factor. Nanofiltration at pH 2.8 and monopolar electrodialysis at pH 4.0 led to increased lactic acid recovery. Moreover, it was observed that process B resulted in 1.09-fold higher lactic acid recovery than process A. However, process A had a 1.19-fold lower specific energy consumption, and the presence of ions in the final solution was reduced by 5-fold. In both processes lactic acid was separated from sugars and organic acids. Overall, the findings of this study suggest that membrane separation technology is a viable method for separating lactic acid produced from a mixture of residual candy-waste and digestate.

1. Introduction

Climate data show that the Earth's surface temperature has increased by 1 ℃ since the start of the industrial revolution, with 2022 being the sixth-warmest year on record [11]. Meanwhile, the human population has tripled compared to the mid-20th century [32], leading to overconsumption and overexploitation of natural resources in producing sufficient energy, fuels, and chemicals [31]. To achieve a greener transition, biorefinery technologies are being developed to valorize biomass to produce bio-energy, bio-fuels, and bio-chemicals [18].

Lactic acid is a bio-chemical mainly generated through microbial fermentation with the application of lactic acid bacteria (LAB) [5]. It is used as a platform chemical for generating products appearing in various sectors, such as food or medical industries [6]. The main factors decreasing the production cost of lactic acid for scaled-up processes are a. the use of an inexpensive substrate with low pretreatment requirements [15], b. the use of a robust microorganism resistant to adverse conditions and fermentation products [5], and c. the optimization of separation and purification strategies.

The most widely used inexpensive biomass for lactic acid production is the lignocellulosic material from agriculture [2] or forest residues [35]. However, the presence of lignin creates the need for pretreatment, increasing the total operational cost [16]. In the search of biomass with low lignin content, organic waste is suggested [3]. Using organic municipal and industrial residues in biorefinery systems creates new value from what was previously considered waste. Meanwhile, the use of organic residues as fermentation resources is suggested as a waste management approach [3]. For example, lactic acid has been produced in a yield of 0.75 $g_{\text{-LA}}\ g^{-1}_{\text{-sugars}}$ and productivity of 1.09 g L^{-1} h^{-1} by source-sorted organic household waste [36], and a yield of 0.98 $g_{\text{-LA}}\ g^{-1}_{\text{-sugars}}$, and productivity of 1.33 g $L^{-1}h^{-1}$ by hydrolyzed cheese whey as carbohydrate sources [38].

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https://doi.org/10.1016/j.jece.2023.110881
Received 15 June 2023; Received in revised form 1 August 2023; Accepted 28 August 2023
Available online 28 August 2023

The downstream strategy should be planned considering the heterogeneity and characteristics of the specific biological substrate. Membrane separation is suggested as a green methodology among other downstream processes as harmful chemicals are not applied, and it is easily up-scaled [1]. Microfiltration (MF) is used for the separation of molecules with molecular weight cut-off (MWCO) > 10,000 Da, such as microbial biomass [1], and nanofiltration (NF) is introduced for molecule separation with MWCO 200–1000 Da [20], such as proteins, macromolecules, and multivalent anions [1,8]. The amount of dissociated lactic acid in the substrate strongly affects nanofiltration. The dissociation constant of lactic acid or pK_a is 3.86 at 25 ℃ [28]. The use of membranes was the first lactic acid purification step applied on fermentation broths deriving from coffee mucilage [24], or from organic fraction of municipal solid waste [21]. The filtration conditions fluctuate depending on the characteristics of the specific substrates.

Electrodialysis (ED) is another membrane separation technology which has received significant attention for the concentration and purification of organic acids [12]. Monopolar ED (MED) is a methodology that utilizes an electric field on ion exchange membranes to concentrate organic acids [12,22]. Bipolar membrane electrodialysis (BPED) is an alternative ED method, where monopolar membranes are combined with bipolar membranes to produce acids and bases from salts (C. [19]. Using BPED, sodium lactate can be converted to lactic acid and sodium hydroxide. In a study conducted by Olszewska et al. [25], lactic acid was produced from sweet sorghum juice, concentrated by MED, and further converted with BPED. In total, 85.6% of the initial lactic acid could be recovered. In another study [27], lactic acid was produced using mixed restaurant food waste as a substrate, and a combination of MF, NF, ED, chromatography, and distillation were applied to recover 38% of the initial lactic acid amount.

Overall, the separation efficiency and the energy consumption of membrane processes depend on the supernatant composition influenced by the applied feedstock media. This study employed a lactic acid solution produced by microbial fermentation of a mixed substrate consisting of candy-waste and digestate that has not been studied before. In lab-scale experiments, two process routes have been compared and evaluated to maximize lactic acid recovery and purity, and minimalize energy consumption. Process A consisted of prefiltration with MF and NF followed by conversion of lactate to lactic acid in BPED. Process B included pretreatment with MF and MED and subsequent BPED.

2. Materials and methods

2.1. Model solution and chemical reagents

A model solution was used for the preliminary experiments, which aimed at optimizing the LA recovery during NF and MED treatment. The solution was formulated based on the properties of the biological MF permeate, which contained 13.70 g L^{-1} maltose, 0.10 g L^{-1} glucose, 0.10 g L^{-1}, succinic acid, 34.31 g L^{-1} lactic acid, and 0.20 g L^{-1} acetic acid. Analytical grade chemicals (Sigma- Aldrich, Darmstadt, Deutschland) were used, and NaCl (99.0%) was added to adjust the conductivity, while HCl (99.8%) or NaOH (98.0%) was used to adjust the pH.

2.2. Biological substrate

The biological substrate (Table 1) was prepared and obtained from the Chemical Engineering Department, Technical University of Denmark (DTU), Kgs. Lyngby, Denmark. The fermentation broth was produced by co-fermenting digestate from a full-scale biogas plant (Hashøj biogas plant, Dalmose, Denmark) and candy-factory waste (*Trolli Ibérica* A/S, Paterna, Spain) and *Lactobacillus plantarum* as seed, in 5-L bioreactors (BioBench, Biostream International BV, Doetinchem, The Netherlands) The substrate selection, pre-treatment, choice of bacterial seed, and fermentation process were previously described by Papadopoulou et al. [26]. The substrate was centrifuged at 4500 rpm for 15 min at 4 ℃ to remove coarse particles, and the liquid fraction was stored at - 20 ℃. Before the membrane separation, the biological substrate was thawed, diluted 1:1 with distilled water, and homogenized for 30 min to increase permeability.

Table 1
Characteristics of the initial fermentation broth diluted 1:1 with distilled water at pH 6.5.

Parameters	Biological sample (g L^{-1})
Total solids (TS)	38.10 ± 0.51
Volatile solids (VS)	23.61 ± 0.24
Glucose	n.d.
Sucrose	n.d.
Maltose	19.55 ± 1.60
Lactic acid	31.30 ± 1.81
Succinic acid	0.30 ± 0.30
Formic acid	n.d.
Acetic acid	0.77 ± 0.52

n.d.: not detected.

2.3. Pressure-driven membrane separation process

MF was applied at a laboratory-scale cross-flow unit (OS-MC-01 OSMO Membrane Systems GmbH, Korntal-Münchingen, Germany) with a 2-L unit tank operated at 2 bar pressure. The unit was equipped with a 0.008 m^2 (0.04 m × 0.2 m) membrane module and a flat sheet MFG2 membrane (Alfa Laval, Lund, Sweden) (Table 2). The system temperature was controlled using a circulating bath (PolyScience 9706A12E Refrigerated/Heated, Manchester, UK) at 60 ℃. The process resulted in two streams: a MF retentate (30% of the feed), which was discarded, and a MF permeate (70% of the feed). The MF permeate was further processed using NF. NF was conducted in the same cross-flow unit at room temperature and 28 bar feed pressure. The unit was equipped with a flat sheet NF245 membrane (FilmTech™, United States) (Table 2). Similar to MF, two streams were produced, a NF retentate (30% of the feed) which was discarded, and a NF permeate (70% of the feed), where lactic acid was accumulated.

In both membrane separation processes, conductivity and pH were monitored every 30 min using the multi-parameter pH-meter VWR pHenomenal® MU 6100 H (VWR International, Vienna, Austria), (Fig. S2). The permeate flux was determined by measuring and recording the permeate mass every 60 min for MF and 25 min for NF using a laboratory precision balance (Kern PKP 4200–2, Precision 0.01 g / max, 4210 g, Reinach, Switzerland). All experiments were performed in batch mode in duplicate, except for NF experiments.

2.4. Electrodialysis

MED and BPED tests were performed in batch mode using the BED 1–3 64004 lab plant (PCCell GmbH, Germany) system. The system consisted of an ED stack with ten cell pairs and an effective membrane area of 0.0064 m^2. For MED, monovalent selective anion-exchange membrane (AEM) and monovalent selective cation-exchange membrane (CEM) were used. The spacer thickness was 0.45 mm. PC MTE cation exchange membranes were used as end membranes. For BPED, bipolar membranes (PCCell GmbH, Germany) were included in the stack. Specifications of the membranes are listed in Table 3. The system had three external double-wall tanks for dilute/ concentrate or feed/ acid/ base and an internal reservoir for the electrolyte rinse solution. The electrolyte rinse solution was 0.25 M sodium bisulfate (Na_2SO_4) and circulated in the system at a flow rate of 120 L h^{-1}. The flow rate of the system for both MED and BPED processes was set at 15 L h^{-1}. The maximum current and voltage that could be applied were 5 A and 30 V, respectively. The voltage remained constant at 30 V, whereas a low current value of 0.4 A (current density: 62.5 A m^{-2}) was applied if either

Table 2
Membrane characteristics, where MF: microfiltration; NF: nanofiltration; experiments.

Flat Sheet Membrane type	Model	Manufacturer	Material	pH rangeRef. 25 ℃	Pore Size-MWCO	Max Temp. (℃)	Max P (bar)
MF	MFG2	Alga Laval	Polypropylene	1.5–12	0.2 μm	75	3
NF	NF245	DOW™	Polyamide-TFC	1.0–10	300 Da	50	54.8

Table 3
Properties of the membranes used for MED: Monopolar electrodialysis; BPED: Bipolar electrodialysis experiments.

	Membrane	Type	Functional Group	Thickness (μm)	Resistance (Ω cm^2)	Transfer number	pH stability
Monopolar electrodialysis	PC MTE	CEM	Sulfonic acid	220	4.5	> 0.94	1–8
	PC MVA	AEM	Ammonium	110	20	> 0.97	0–9
	PC MVK	CEM	Sulfonic acid	100	n.a.	> 0.97	0–10
Bipolar	PC MTE	CEM	Sulfonic acid	220	4.5	> 0.94	1–8
electrodialysis	PC acid 60	AEM	Ammonium	100–110	2	> 0.95	0–9
	PC SK	CEM	sulfonic acid	100–120	2.5	> 0.95	0–11
	PC bip	BP	bipolar	200–350	-	> 0.95*	0–12

n.a.: not available.
* Water-splitting efficiency

concentrate or dilute electrical conductivity (EC) was below 5 mS cm^{-1}. The applied current densities (CD) were selected based on prior experiments and were approximately 50% of the LCD (Limiting Current Density) obtained at these concentration levels (Fig. S3). However, if the EC of both streams was above 5 mS cm^{-1}, a higher value of 0.7 A (110 A m^{-2}) was used. All experiments were finalized when an EC of 5 mS cm^{-1} was achieved in the feed solution. EC, temperature, and pH were continuously monitored and recorded (Fig. S2). All experiments were performed in duplicate. The experimental time, specific energy demand, and lactic acid recovery were considered during the evaluation of experimental results.

2.5. Experimental set-up

To achieve maximum recovery of high-purity lactic acid while minimizing energy consumption, selected membrane processes were optimized (Table 4). The factor studied and controlled was the pH, which affects both NF and MED methods. The pK_a of lactic acid was estimated to be 3.86 at 25℃ [28]. Considering this information, three pH conditions were tested to investigate how the dissociation of lactic acid affects the separation by membrane technology. Therefore, pH 4.0 was selected as a value close to the dissociation constant, while pH 2.8, a value lower than the pK_a, was chosen based on a previous study [8], which indicated that it was the optimal pH for lactic acid separation following the NF process. All three pH conditions were evaluated for affecting the MED process, utilizing the model solution. However, only two pH conditions, pH 2.8 and 6.5, were applied for the NF process, as previous research on the separation of model lactic acid solution [8] demonstrated that these two values exhibited the greatest differences. The initial pH of the model solutions, which was approximately 2.0, was adjusted by adding NaOH until the desired pH (2.8, 4.0, or 6.5) was obtained. NaCl was added to reach an equal EC of 15 mS cm^{-1} for all the solutions, representing the EC of the original fermentation effluent. Initially, the dilute container was filled with 400 mL of the test solution, while the concentrate was filled with 400 mL of deionized water.

Additionally, fed-batch experiments were conducted at pH 4.0 with a model solution to increase the purity and concentration of the lactic acid solution. Diluate and concentrate containers were filled with 400 mL of lactic acid model solution and deionized water. After the first batch experiment, the diluate was replaced with a new model solution while reusing the obtained concentrate. In total, three fed-batch experiments were performed in duplicate. The experimental time, specific energy demand, and LA recovery were considered for the evaluation of the results.

Experiments with biological samples were conducted as a validation step to determine the best process design (Fig. 1). First, the fermentation broth was diluted 1:1 with distilled water to allow permeability through the membrane, and it was used as a feed for the pre-purification step. The MF permeate was then used either in process A, as a feed for either NF or in process B, as feed for MED, operating at the selected pH found in the preliminary experiments. The NF permeate, and the MED concentrate were tested as feed solutions for BPED.

2.6. Analytical methods

Sugars (maltose and glucose) and organic acids (lactic, succinic, and acetic) were detected and measured with High-Performance Liquid Chromatography (HPLC). The HPLC unit was equipped with a refractive detector and a Shodex SH1011 (8.0 mm × 300 mm) column, operating at a column oven temperature of 60 ℃. Eluent was 5 mM H_2SO_4, and

Table 4
Experimental design for the optimization of the lactic acid downstream process.

Separation method	Substrate	Pressure (bar)	Temperature (C)	pH	Current (A)	Voltage (V)
MF	Biological diluted 1:1	2	60	6.5	-	-
NF	MF permeate	28	25	2.8	-	-
				6.5		
MED	Synthetic	-	22.17 ± 0.80	2.8	0.7	30
				4.0		
				6.5		
	MF permeate		22.85 ± 0.65	n.a.		
MC	Synthetic		23.29 ± 1.01	n.a.		
BPED	NF permeate	-	24.75 ± 0.15	n.a.	0.4	30
	MED concentrate		24.05 ± 1.05	n.a.	0.7	30

n.a.: Not available.

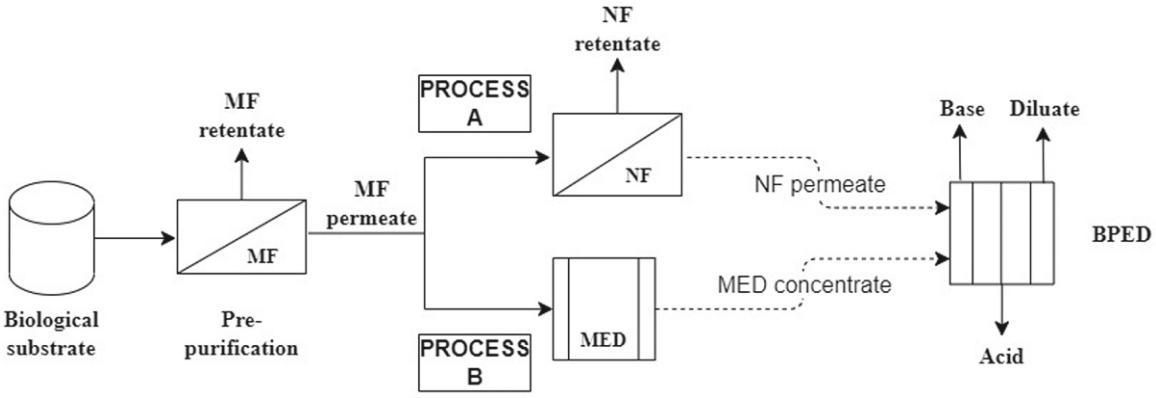

Fig. 1. Experimental set-up for maximum lactic acid recovery and purity.

analysis was conducted with a 0.6 mL min^{-1} flow rate. Before the analysis, the samples were centrifuged at 10,000 rpm for 10 min, and the supernatant was diluted with distilled water. The samples were filtered with non-sterile 0.22 μm pore size filters (Dissolution accessories, Munich, Germany) into the glass vials.

Anions (chloride, sulfate) and cations (sodium, potassium, calcium, and magnesium) were analyzed according to DIN EN ISO 14911 by HPLC. The limit of quantification (LOQ)/ limit of detection (LOD) was 0.5/ 0.2 mg L^{-1} for anions and 0.8/ 0.4 mg L^{-1} for cations.

3. Calculations

3.1. Lactic acid recovery and purity

Lactic acid recovery (R) (Eq. 1), and purity (P) (Eq. 2) were calculated as yields for all separation strategies.

$$R(\%) = \left(\frac{M_p^{LA}}{M_f^{LA}}\right) \times 100 \quad (1)$$

$$P(\%) = \frac{M_p^{LA}}{M_p} \times 100 \quad (2)$$

Where: M_p^{LA} – mass of lactic acid in the permeate or in the diluate for filtration and ED strategies, accordingly; – M_f^{LA}mass of lactic acid in the feed; M_p – mass of sugars and organic acids recovered after downstream.

3.2. Microfiltration and Nanofiltration

The pump power (Eq. 3) and the final volume of the permeate were considered for the calculation of the specific energy consumption (SEC) (Eq. 4). Pump power is characterized as the pressure needed to pump the feed in the system.

$$P_p = \frac{Q_{Uf} \times P_U}{\eta} \quad (3)$$

$$SEC = \frac{P_P}{Q_{Up}} \quad (4)$$

Where P_P: pump power (W), Q_{Uf}: feed flow (m^3 s^{-1}), P_U: pressure (Kg m^{-1} s^{-1}), η: pump efficiency (0.75), Q_{Up}: permeate flow (m^3 s^{-1}).

In the MF process, the energy consumption for the temperature control of the thermal bath was also considered (Eq. 5). The temperature of the system was set at 60 °C.

$$Q = m \times c \times \Delta T$$

Where *m*: mass (kg), *c*: specific water heat (4.180 $\times 10^3$ J kg^{-1} $°C^{-1}$), ΔT: temperature (°C).

The capacity of the circulating bath was 13-L capacity but only 3 L were used for heating.

3.3. Electrodialysis

The electrical power $P_{ED,t}$ and cumulative electrical energy demand E_{ED} were calculated according to Eq. 6, and Eq. 7.

$$P_{ED,t} = U_t \times I_t \quad (6)$$

$$E_{ED} = \sum_{n=0}^{t} P_{ED,t} \quad \times (t_{n+1} - t_n) \quad (7)$$

Where: U_t – recorded voltage; I_t – applied current; t – desalination time.

Power for pumping P_P was calculated based on Eq. 8. The observed pressure drop was approximately 0.5 bar at a chosen flow velocity of 15 L h^{-1} for the feed, concentrate/acid and base pump, and 120 L h^{-1} for the electrolyte pump.

$$P_p = V \times \rho \times \Delta p \quad (8)$$

where: V – volume flow; Δp – pressure-drop; ρ– density of the water matrix.

The energy demand for pumping E_P was the product of pumping power, time, and n the number of pumps needed (diluate pump, concentrate pump, base pump/electrolyte pump) divided by the pump efficiency (for all pumps an efficiency of $\eta = 0.8$ was assumed) and described in Eq. 9.

$$E_P = \frac{P_p \times t \times n}{\eta} \quad (9)$$

The total cumulative energy demand E_{total} is the sum of the electrical energy demand for desalination and the energy demand for pumping (Eq. 10). SEC was also calculated according to Eq. 4.

$$E_{total} = E_{ED} + E_p \quad (10)$$

Furthermore, the recovery efficiency of lactic acid (RE_{LA}) was assessed using initial and final masses within the diluate compartment (Eq. 11).

$$RE_{LA} = \frac{m_{D,i}^0 - m_{D,i}^f}{m_{D,i}^0} \times 100 \quad (11)$$

where $m_{D,t}^0$, $m_{D,i}^f$ – initial and final mass in the diluate compartment.

4. Results and discussion

To determine the optimal downstream process for achieving maximum recovery of high-purity lactic acid from a fermentation broth

derived from a mixture of residual streams, two membrane processes were designed. Firstly, the pH was tested and optimized as a factor that could potentially influence the separation of lactic acid during the implementation of NF or MED technology. Subsequently, MF was applied as a pre-purification step and two downstream processes were suggested. Process A involved a NF step followed by BPED, while process B combined MED and BPED. Finally, a fed-batch MED operation was examined as a method for up-concentration of lactic acid.

4.1. pH effect of NF and MED processes

Two sets of NF experiments were conducted to investigate the influence of pH on lactic acid separation process. In the first set the pH of the biological substrate remained unaltered at 6.5, whereas in the second case the pH was reduced to 2.8. When the pH was 6.5, 27.22% lactic acid was recovered, and 3.58% of maltose was found in the permeate (Fig. 2). Altering the pH to 2.8 led to a 1.64-fold increase in lactic acid recovery, but also a 3.70-fold higher amount of maltose was recovered, reducing the purity of lactic acid.

The pH of the feed solution in NF processes has been reported to affect the charge of the membrane, which is dependent on the membrane's isoelectric point. For instance, research has shown that the isoelectric point of NF245 membrane, which was also used in this study, is close to 4.0 [7]. At pH levels higher than 4.0 the membrane becomes negatively charged. As lactic acid is also negtively charged, a greater amount of lactate is detected and retained in the retentate, instead of being recovered in the permeate.

The recovery rate of lactic acid separated from the biological substrate in the selected pH ranges was comparable to the results previously reported by Cabrera-González et al. [8], operating also in laboratory scale, using a model solution of lactic acid. According to their research, lactic acid recovery rates ranged from 0% to 20% at pH 6.0, while at pH 2.8 the recovery rates increased to ranges between 29% and 93%, depending on the characteristics of the employed membranes.

However, a study presented by Alexandri et al. [1] demonstrated a fermentation process using residue substrates, combined with NF as downstream technology, resulting in lactic acid recovery yields ranging from 77.6% to 97.5%. In contrast, the sugar recovery rates were found to be in the range of 63–100%, similar to those achieved in the current study. The variation in lactic acid recovery rates observed between the two studies can be attributed to several factors, including differences in membrane area, substrate composition, and membrane characteristics. An important distinction between the two studies, is that Alexandri et al. [1], conducted NF experiments on a pilot scale, utilizing a membrane area that was 213-fold larger than the one used in the current study.

Furthermore, disparities in substrate composition between the two studies could also play a role. Alexandri et al. [1] employed residue substrates with an average disaccharide concentration that was 1.9-fold lower compared to the samples used in the present study. Such differences in substrate composition can impact the performance of the membrane separation process. Finally, variations in the characteristics of the membranes utilized in the two studies may also contribute to the differences in lactic acid recovery rates. Some differences could arise due to membrane permeability, selectivity, or surface charge, which can affect the separation efficiency.

An additional contributing factor to the decrease in the reported lactic acid amount was the presence of process losses, constituting approximately 18.53% of the initial mass, regardless of the chosen pH. Process losses have been previously observed and reported [4]. However, in this specific study, the percentage of process losses appears to be higher compared to the previously reported range of 6–7%. Despite this difference, the consistency of these process losses was observed throughout the repeated experiments.

The effect of pH on the MED process was also studied, and the results (Fig. 2) indicated that lactic acid recovery was highest at pH 4.0, with a 1.05-fold increase compared to pH 2.8 and 6.0. Additionally, the experimental time, electrical, pumping, and electrical energy demand decreased with increasing pH value (Table 5). These results could be attributed to the fact that when the pH of the feed is lower than 3.86, lactic acid will remain undissociated in the diluate compartment [28]. Conversely, if the pH is regulated at higher values, the lactate anion will mitigate in the concentrate compartment. In a previous study on removing lactic acid from acid whey [10], no significant differences were found in lactic acid removal and specific energy consumption between pH 4.6 and 6.0 at temperatures between 30 and 45 °C. However, the present study discovered that at pH 6.0, the specific energy

Table 5
Energy characteristics for different pH conditions applied on monopolar electrodialysis (MED) technology.

pH	Initial volume diluate (L)	ΔEC_d (mS cm^{-1})	Exp. Time (h)	Electrical energy (Wh)	Pumping energy (Wh)	Specific energy demand (kWh m^{-3})
2.8	0.289 ± 0.015	13.13 ± 0.14	1.74 ± 0.01	11.6 ± 0.4	1.8 ± 0.0	46.6 ± 2.1
4	0.292 ± 0.177	15.18 ± 3.10	1.17 ± 0.02	9.5 ± 0.3	1.2 ± 0.0	36.8 ± 3.1
6.5	0.308 ± 0.092	13.99 ± 0.45	0.96 ± 0.07	7.1 ± 0.7	1.0 ± 0.1	26.2 ± 0.5

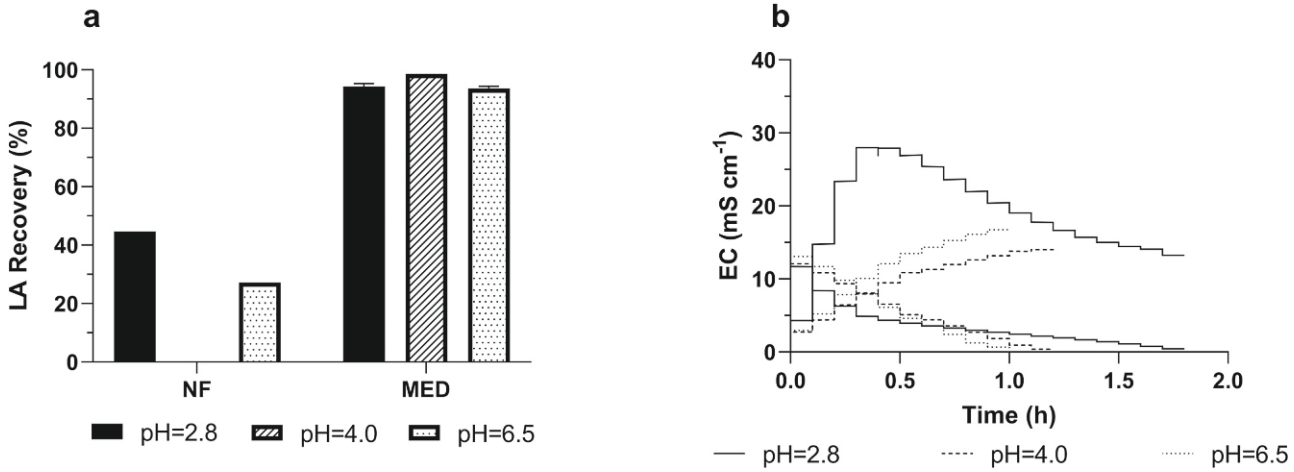

Fig. 2. pH effect on nanofiltration (NF) and monopolar electrodialysis (MED) technologies. Plot a. shows the lactic acid recovery (%) in each studied pH and plot b. shows the fluctuation of electric conductivity (EC) in the diluate and the concentrate, in different pH values.

consumption was 1.4 times lower than in pH 4.0. In general, the more dissociated the lactic acid, the less energy is required to separate lactic acid into ion form, while most of the energy is used to facilitate ion transfer [28]. Considering both the high lactic acid recovery and the reduction in energy demand, the pH of 4.0 was selected to continue with the MED experiments.

4.2. Maximum recovery of high-purity lactic acid using membrane separation technologies

The fermentation broth utilized in this study was derived from a co-fermentation of candy- waste and digestate. Candy-factory residues contain impurities of high molecular weight, such as gelatin and sugars [17]. The addition of high sugar concentration in gelatin systems has been found to increase the initial melting point of gelatin (≈ 35 °C) (R. [34]. Thus, to decrease the viscosity and turbidity of the substrate, a first MF separation step with 0.2 μm filters was proposed as a common pre-purification step [17]. Furthermore, to minimize a potential flux reduction caused by gelling behaviour of the substrate, the tank temperature was set at 60 °C. The applied temperature was not optimized.

The results (Table 6, Fig. 3) demonstrate that the MF technique allowed for the recovery of 73.27 ± 1.07% of the compounds present in the fermentation broth. The average purity of lactic acid obtained was 59.20 ± 2.63%. The lactic acid losses observed here are comparable with previous findings involving heterogeneous substrate, such as crust bread [1]. However, the observed losses were higher by 1.15- to 1.36-fold when compared to other substrates such as sugar bread and acid whey, respectively. The variability in rejection rates among different substrates, as discussed by Alexandri et al. [1], suggests that substrate characteristics play a significant role in influencing lactic acid losses during the MF process.

Furthermore, the permeate flux for MF was also monitored, and it exhibited a decrease over time, with a 13.5% reduction observed after 3 h (Fig. S1). This phenomenon can be attributed to membrane fouling from the fermentation broth [1]. Cross-flow MF, as the one applied in this study, is known for effectively controlling the disposition of bacterial cells to the membrane surface, resulting in a relatively constant permeate flux of 37 kg m^{-2} h^{-1} [29], which is consistent with the one obtained in this study.

Finally, the SEC for the process was calculated to be 0.10 kWh m^{-3}. Comparatively a typical MF process requires 0.18 kWh to produce 1 m^3 of water [30]. In a previous study by Najid et al. [23] the SEC was estimated to be nearly constant at approximately 0.086 kWh m^{-3}, which is comparable to the results presented in this study.

Subsequently, the MF permeate was directed either for NF at pH 2.8, or MED at pH 4.0. The results (Fig. 3) showed when MED was used, 2.14-fold more lactic acid was recovered, and the purity was 1.15-fold higher than that obtained with the NF process. Moreover, when NF was used, 3.09-fold more maltose was recovered. However, the SEC for MED was 23-fold higher than that for NF. Both technologies achieved decolorization of the permeate and concentrate, respectively (Fig. S4). This aligns with literature reporting on high decolorization rates achieved by nanofiltration membranes [9]. During MED experiments, the concentrate tank was initially filled with deionized water. Macromolecular compounds such as pigments and proteins are retained via the perm-selectivity of IEX membranes and will rather remain in the diluate compartments due to the small membrane pore sizes (<1 nm) [37].

The application of BPED to the NF permeate or MED concentrate resulted in the complete separation of lactic acid from residual sugars and organic acids in the fermentation broth. The recovery of lactic acid was 1.09-fold higher when MED concentrate was used as BPED feed compared to the NF permeate. On the other hand, the combination of NF and BPED reduced the specific energy consumption of the process by 4.54-fold, compared to the combination of MED and BPED (Table 7). In a similar study conducted by Knežević et al. [14] NF, MED, and ion-exchange membranes were applied for ion removal from fermentation eluent, before the application of BPED. The energy demand calculated for NF was 1.06 kWh m^{-3}, which is comparable with the present study. However, the energy demand recorded for MED in this study was almost 2.5-times higher than the one reported from Knežević et al. This deviation could be attributed to the fact that in the study of Knežević et al., the current density was almost half compared to the one applied in this study.

Regarding ion concentration (Table 6), it was detected that the MED concentrate contained 3.07-fold more ions than the NF permeate. After the BPED process, 6.02-fold more ions were detected in Process B than in Process A. These findings were also supported by the calculation of the ion removal efficiencies obtained during the applied ED processes on the biological sample (Table S1). According to the results, in process A, complete removal of SO_4^{2-} and K^+ ions was achieved, while Cl^- and Na^+ ions were partially removed by 93.74 ± 1.88% and 90.36 ± 2.32%, respectively. The removal efficiency of lactic acid from the diluate

Table 6
Concentration of organic acids (lactic, succinic, acetic), sugars (maltose, glucose), and ion found in each stage of the lactic acid separation process.

Fermentation broth	Diluate mass (g)	LA (g L^{-1})	SA (g L^{-1})	AA (g L^{-1})	Mal (g L^{-1})	Glu (g L^{-1})	Cl^- (mg L^{-1})	SO_4^{2-} (mg L^{-1})	Na^+ (mg L^{-1})	K^+ (mg L^{-1})	Ca^{2+} (mg L^{-1})	Mg^{2+} (mg L^{-1})
MF Retentate	379.60 ± 87.59	39.31 ± 3.21	1.04 ± 0.23	1.34 ± 0.17	23.25 ± 0.96	n.d.	142.5	74.5	5350	812	28.9	7.5
MF Permeate	1569.58 ± 124.78	28.98 ± 2.77	0.41 ± 0.41	1.24 ± 0.18	17.71 ± 0.99	n.d.	160.5	151.2	4560	257	23.9	6.5a
NF Retentate	526	27.3	n.d.	n.d.	27.26	n.d.	173.3	12262	8051	515	56.1	9.9
NF Permeate	1099	16.7	n.d.	n.d.	3.33	n.d.	94.1	114.8	721	20.9	0	0
MED Diluate	444.93 ± 7.39	1.33 ± 0.16	n.d.	n.d.	35.22 ± 12.52	n.d.	35.50 ± 24.61	n.d.	165.00 ± 25.45	n.d.	6.00 ± 0.00	1.50 ± 0.71
MED Concentrate	440.98 ± 0.25	37.18 ± 3.65	n.d.	0.14 ± 0.20	1.26 ± 0.69	n.d.	4592.00 ± 214.96	171.80 ± 21.64	3037.50 ± 67.18	208.00 ± 60.81	17.20 ± 1.27	n.d.
NF_BPED Diluate	466.23 ± 5.06	6.14 ± 0.13	0.07 ± 0.07	n.d.	n.d.	n.d.	14.85 ± 0.49	n.d.	49.55 ± 7.85	n.d.	n.d.	n.d.
NF_BPED Acid	466.40 ± 2.47	15.46 ± 0.30	n.d.	n.d.	n.d.	n.d.	411.55 ± 222.53	216.90 ± 16.69	90.55 ± 30.33	n.d.	n.d.	n.d.
NF_BPED Base	466.25 ± 1.70	1.04 ± 0.31	0.07 ± 0.07	n.d.	n.d.	n.d.	48.65 ± 6.29	15.85 ± 1.34	513.00 ± 67.88	15.40 ± 4.10	1.50 ± 2.12	n.d.
MED_BPED Diluate	452.83 ± 30.16	4.49 ± 0.39	n.d.	n.d.	n.d.	n.d.	22.45 ± 2.19	14.15 ± 7.99	126.65 ± 8.98	2.45 ± 3.46	n.d.	n.d.
MED_BPED Acid	452.90 ± 29.42	19.24 ± 2.55	n.d.	n.d.	0.56 ± 0.42	n.d.	3291.50 ± 1009.04	142.10 ± 25.60	348.50 ± 146.37	n.d.	n.d.	n.d.
MED_BPED Base	451.45 ± 33.52	0.81 ± 0.03	n.d.	n.d.	n.d.	n.d.	286.40 ± 224.86	30.50 ± 1.56	2600.00 ± 70.71	103.05 ± 4.31	14.40 ± 2.26	5.00 ± 7.07

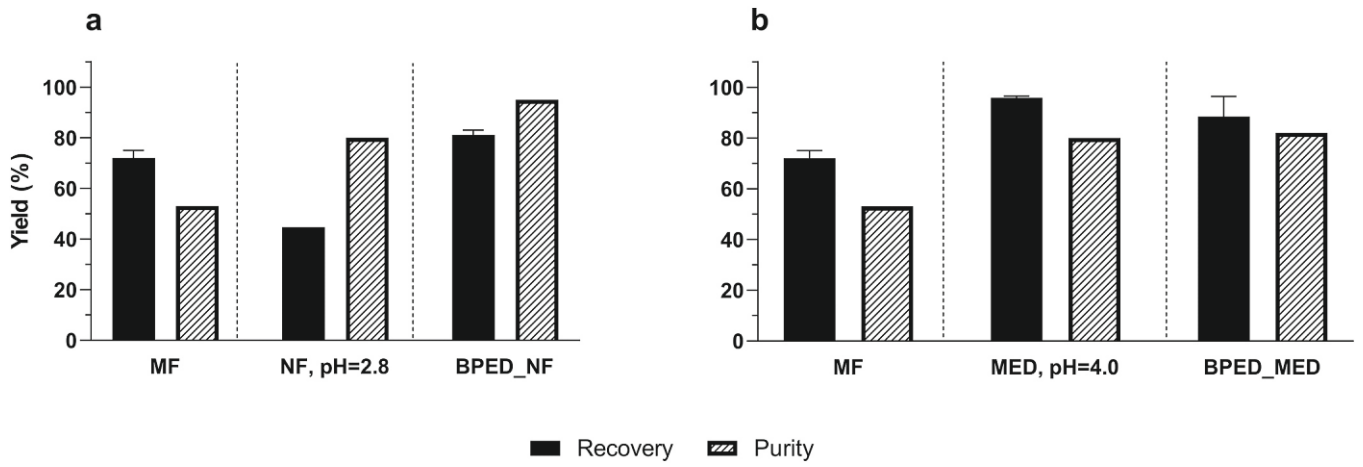

Fig. 3. Lactic acid recovery and purity as yields for process A: microfiltration (MF)-Nanofiltration (NF)-Bipolar Electrodialysis (BPED), and for process B: microfiltration (MF)-Monopolar electrodialysis (MED)-Bipolar Electrodialysis (BPED).

Table 7
Energy consumption for the pre-purification process, and the two proposed downstream processes, A: microfiltration (MF)-Nanofiltration (NF)-Bipolar Electrodialysis (BPED), and B: microfiltration (MF)-Monopolar electrodialysis (MED)-Bipolar Electrodialysis (BPED).

	Membrane Process	Initial mass diluate (g)	ΔEC_d (mS cm^{-1})	Exp. Time (h)	Electrical energy (Wh)	Pumping energy (Wh)	Specific energy demand (kWh m^{-3})
Process A	MF	1304 ± 81.99	16.453 ± 1.351	3.33	-	0.137 ± 0.01	0.106
	NF_ pH 2.8	660	1.8	0.83	-	0.943	1.416
	NF_ BPED	466.23 ± 5.06	1.44 ± 0.32	0.38 ± 0.14	5.61 ± 2.47	0.30 ± 0.11	12.03 ± 5.17
Process B	MED_ pH 4.0	444.93 ± 7.39	12.81 ± 1.05	1.17 ± 0.13	14.46 ± 1.78	0.61 ± 0.07	32.56 ± 4.58
	MED_BPED	452.83 ± 30.16	11.10 ± 0.47	0.66 ± 0.05	12.86 ± 0.32	0.51 ± 0.04	28.45 ± 1.20

compartment was measured to be 81.10 ± 1.39%. In contrast, for process B, the highest ion removal efficiencies were observed for Cl^-, K^+, and Na^+ ions, with removal rates of 99.28 ± 1.39%, 99.25 ± 0.75%, and 97.97 ± 0.11%, respectively. The lowest ion removal efficiency was recorded for SO_4^{2-}, which reached 88.96 ± 6.04%. Notably, the removal of lactic acid in process B was higher compared to process A, with a 1.18-fold increase in lactic acid removal. Previous studies have shown that the application of NF technology yields a solution free of Ca^{2+} and Mg^{2+} [4], while MED removed only Mg^{2+}, potentially due to lower atomic weight. The residual Ca^{2+} concentration in the MED concentrate was 17.20 ± 1.27 mg L^{-1}, thus higher than the recommended concentration of 10 mg L^{-1}. This could evolve to be a problem because calcium can precipitate on the bipolar membranes forming an insoluble $Ca(OH)_2$ layer. Finally, after completing the downstream process K^+, Ca^{2+} and Mg^{2+}, were fully separated from lactic acid and transported to the base compartment. The main contaminants were Cl^-> $SO4^{2-}$>Na^+ for Process A and Cl^-,>Na^+>$SO4^{2-}$ for Process B. It should be highlighted that NaOH was used to set the initial pH of the fermentation broth from 6.5 to 4.0 and 2.8, for MED and NF, respectively.

Additionally, measurements of the removal of proteins, phosphate ($PO4^{3-}$), and ammonium (NH_4^+) compounds should have been considered for improving the understanding of lactic acid purity. However, it was a limitation of this study that these parameters were not considered. Considering the results obtained from a previous laboratory-scale study [4] the removal of 20% nitrogen and 25% phosphorus compounds was detected after the pre-purification process, including centrifugation, ultrafiltration, and activated carbon treatment. Following the pre-purification step 59–61% of nitrogen, and 80–82% of phosphorus were rejected when NF was applied. Another study conducted by Alexandri et al. [1] showed that 39.9–77.5% total nitrogen and 55.8–98.8% total phosphorus were rejected after the application of an MF and an NF step, depending on the characteristics of the initial feed. Another study by Knežević et al. [14] comparing ion removal from waste fermentation effluent, comparing NF, MED, and IEX for the recovery of sulfuric acid studied the permeability of NH_4^+ and $PO4^{3-}$. According to this research the concentration of NH_4^+ was reduced 1.42- to 2.74-times, applying NF, depending on the characteristics of the membrane. On the contrary, the NH_4^+ concentration was increased by 1.55-times, when applying MED. After the BPED step the excess NH_4^+ is collected to the base compartment creating ammonium hydroxide (NH_4OH). The concentration of $PO4^{3-}$ was also decreased by 1.19- to 1.38-fold when applying NF, and increased by 1.53- to 1.60-fold when running MED. $PO4^{3-}$ would be transferred to the acid compartment, during a BPED, creating phosphoric acid (H_3PO_4).

Previous studies have been conducted (Table 8) on the downstream of lactic acid deriving from the fermentation of residual streams [1,4,24]. In a study separating lactic acid from municipal biopulp [4], ion exchange (IE) technology or a combination of IE and NF were used. The pre-purification step, which was centrifugation and ultrafiltration, led to complete color removal. Furthermore, 80% of lactic acid was recovered through IE. Additionally, the NF step before IE resulted in 73–74% lactic acid recovery and 75–76% removal of divalent ions. Vacuum distillation was used to convert lactate to lactic acid and the overconcentration of the final product. In another study conducted by Neu et al. [24], several separation technologies, including MF, NF, dialysis, a softening step, MED, BPED, decolorization and distillation, were used for the separation of lactic acid from a fermentation broth derived by coffee mucilage. This combination led to a 38.2% lactic acid recovery and 99.8% purity at the end of the process. Finally, Alexandri et al. [1] applied MF and NF as primary separation steps of lactic acid from a fermentation broth

Table 8
Comparison of study findings with previous literature regarding downstream processes for the separation and purification of lactic acid from heterogeneous fermentation substrates. Where ED: electrodialysis; IEX: ion exchange chromatography; LA: lactic acid, Lab: Laboratory; MF: microfiltration; NF: nanofiltration; n.r.: not reported; VD: vacuum distillation.

References	Scale	Feed	Separation technology	LA recovery (%)	LA purity (%)	Final LA (g L-1)
Neu et al. [24]	Pilot	Coffee mucilage	Filtration+ ED+ IEX+ Distillation	38.20	n.r.	930
Pleissner et al. [27]	Pilot	Restaurant food waste	Filtration+ ED+ IEX+ Distillation	38.00	n.r.	702
Alexandri et al. [1]	Pilot	Glucose Acid whey Sugar bread Crust bread	MF NF	78.5–100 77.6–97.5	44.2–77.6	29.7–76.6
Alvarado-Morales et al. [4]	Lab	Municipal biopulp	Filtration+ IEX+ VD Filtration+ NF+ IEX+ VD	75.70 65.00	72.5 82.5	12.12 10.39
Case study	Lab	Candy-waste & digestate	Process A Process B	26.00 61.00	95 82	114

produced by sugar and crust bread. They achieved high lactic acid recovery ranging between 2.5% and 22.4% after NF, despite the decreased purity of 77.6%. In these studies, the energy demand of the processes was not reported. In the present study, 26% recovery and 95% purity were reported for process A, and 61% recovery with 82% purity were achieved for process B. For processes A and B, the SEC was 13.55 and 61.12 kWh m^{-3}, respectively.

4.3. MED application for concentrating lactic acid

Fed-batch MED experiments were conducted to increase the final lactic acid concentration. The experiments were conducted with a model solution at pH 4.0 (Table 8, Fig. 4) to test if and how much lactic acid can be concentrated. After repeating MED three times, lactic acid concentration reached 2.31 times higher concentration than the initial solution, reaching up to 114.88 g L^{-1} (Fig. 4). In a previous study conducted on the purification of organic acids utilizing electrodialysis processes (Q. [33] a final lactic acid concentration of 153 g L^{-1} was achieved, starting from 27.5 g L^{-1}. The strategy applied was a multistage batch of three repetitions, where the volume ratio between diluate and concentrate was increased up to 1:10.

Diluate volumes, EC of the diluate, and removal efficiencies were in a similar range for all three MED rounds (Table 9, Table S2). However, it is visible that during the second and third fed-batch, the total energy consumption was approximately 33–44% lower than within the first step. The higher EC value in the concentrate at the beginning of the MED batch reduces the stack's total resistance, and process efficiency is thus increased.

Table 9
Energy consumption during the different stages of the fed-batch monopolar electrodialysis for the over-concentration of lactic acid.

Step	EC concentrate (mS cm^{-1})		EC diluate (mS cm^{-1})		Exp. time (h)	Total Energy Demand (Wh)
	Initial	final	initial	final		
step1_A	0.14	14.7	12.91	0.33	1.04	10.2
step2_A	14.32	22.44	10.82	0.31	0.89	7.02
step3_A	21.9	28.51	10.87	0.34	0.82	6.87
step1_B	1.17	14.05	13.07	0.34	1.16	10.48
step2_B	13.01	23.09	12.75	0.34	0.93	7.04
step3_B	22.55	28.94	12.64	0.3	0.78	6.03

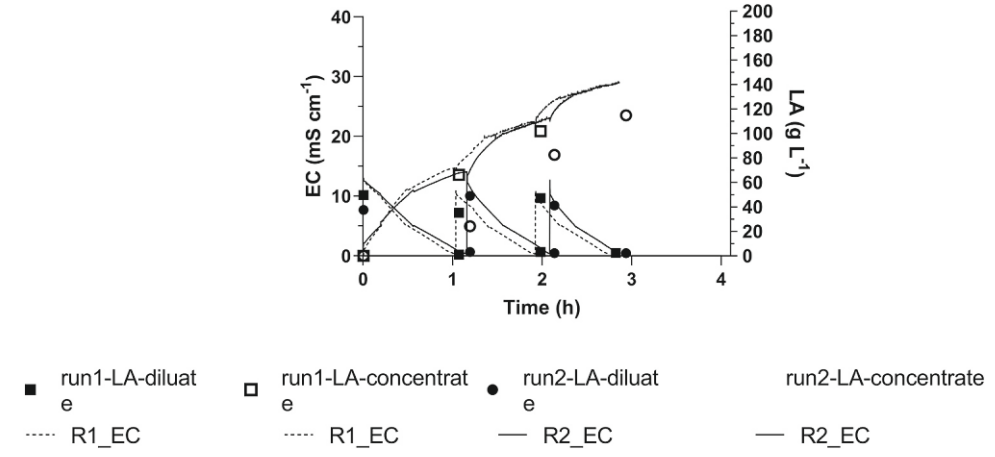

Fig. 4. Electric conductivity and lactic acid concentration variations after three stages of fed-batch monopolar electrodialysis for lactic acid over-concentration.

4.4. Choice of process route and future process optimization

The choice of the process routes depends on process and product requirements. Although the energy demand during single-step MED was higher than for NF; the higher recovery rates are a valid reason to suggest process route B for the downstream treatment of lactic acid-containing solutions. Developing a fed-batch ED process, where lactic acid remains in the retentatecan be recycled, increases the overall yield and decreases the total energy demand [10]. This has been shown in the multiple concentration experiments where energy demand decreased with the number of batches treated to the lower total resistance in the ED stack.

The suggested concept includes pre-treatment with MF, pre-concentration with MED in fed-batch operation, and conversions of lactate to lactic acid using BPED. To ensure ion retention, implementing an IE resin step before BPED would probably be beneficial for process safety. The base (NaOH) stream produced from BPED can be used as a pH control agent to reduce the need for fresh NaOH, resulting in lower upstream process cost [13]. Finally, the additional water obtained from BPED dilute can be used for substrate pre-treatment in the upstream process, e.g. for dilution of the initial solution before MF filtration.

If NF is chosen, comprehensive trials of NF membranes with different properties are proposed [8].

Overall, these approaches can improve the efficiency and sustainability of the downstream process of lactic acid, making its production more economically viable and environmentally friendly.

5. Conclusions

Challenges such as low product purity, low recovery, and high energy demand should be addressed to develop a lactic acid biorefinery. This study emphasizes the importance of regulating parameters such as pH to optimize membrane technologies for the desired bio-product. In the case of lactic acid, pH values of 2.8 and 4.0 were the most suitable for separation via NF and MED, respectively. Additionally, Process B where MED was combined with BPED, resulted in a 1.09-fold increase in lactic acid recovery compared to Process A, where NF was combined with BPED. However, process B showed a specific energy demand 4.51 times higher than process A, and a 6.02-fold higher number of ions remained in the final solution. Finally, the application of fed-batch MED increased lactic acid concentration from 43.70 to 114 g L^{-1}, which is promising for industrial applications. According to our results, downstream treatment by MF, multiple MED and BPED is proposed. Overall, this study provides an optimized strategy for the downstream processing of lactic acid derived from microbial fermentation of heterogeneous residual streams with high sugar content.

CRediT authorship contribution statement

Eleftheria Papadopoulou: Conceptualization, Methodology, Validation, Visualization, Formal analysis, Investigation, Data curation, Writing – original draft. **Mayuki Cabrera-Gonzalez**: Conceptualization, Methodology, Validation, Visualization, Formal analysis, Investigation, Data curation, Writing – original draft. **Daniela Reif**: Conceptualization, Methodology, Validation, Visualization, Formal analysis, Investigation, Data curation, Writing – original draft. **Amal Ahmed**: Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision. **Panagiotis Tsapekos**: Conceptualization, Writing – review & editing, Supervision, Project administration. **Irini Angelidaki**: Conceptualization, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Michael Harasek**: Conceptualization, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Irini Angelidaki, Michael Harasek reports financial support was provided by Europe Horizons.

Data Availability

Data will be made available on request.

Acknowledgments

This work was supported by the European Union's Horizon 2020 – Marie *Skłodowska-Curie* research and innovation program (grant agreement No 860477). The authors would like to express their gratitude to Matthias Hainz, Laura Daza-Serna, Camila Cabeza, Alexandra Nastouli, and Thomas Jung for their invaluable assistance in the lab work and sample analysis. Furthermore, the authors would like to acknowledge and thank the lab personnel of the Institute for Water Quality management for their valuable support during chemical analysis. The authors acknowledge also TU Wien Bibliotek for financial support through its Open Access Funding Program.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jece.2023.110881.

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Production of *Chlorella vulgaris* using grass silage juice and secondary effluents from lactic acid recovery through pressure-driven membranes

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Highlights

- Membrane processes were used to recover lactic acid from grass silage juice
- After nanofiltration, lactic acid was concentrated but recovery was low
- Secondary effluents from lactic acid recovery were used to grow microalgae
- The stream rich in lactic acid and poor in sugars was the best for algae growth
- Simultaneous lactic acid recovery and microalgae growth were shown possible

Abstract

The use of membrane processing to recover organic compounds, such as lactic acid, from grass silage juice is still under development and can be valuable for implementing a green biorefinery. Microfiltration and nanofiltration reached a rejection of 98% of fructose, glucose, and citric acid in a multistage process. Additionally, the rejection of heavy metals was somewhat achieved. However, a low recovery and purity of lactic acid were obtained in the final stream, probably due to the low pH of the grass silage juice used. Secondary effluents rich in organic and inorganic compounds are obtained from the membrane processes. Such effluents are not widely used but their valorization could minimise waste production. Therefore, this study also investigated the application of these secondary effluents for microalgae production. Even though the presence of sugars increased the growth rate of *Chlorella vulgaris*, it also resulted in contamination in most of the tested conditions. The nanofiltration permeate, rich in lactic acid and low in sugars, resulted in the best algae growth and highest chlorophyll production.

Keywords: Lactic acid, Microfiltration, Nanofiltration, Sustainable microalgae cultivation, Circular economy

1 Introduction

The EU bioeconomy strategy outlined measures to promote the establishment of innovative and environmentally friendly biorefineries [1]. Depending on the used feedstock, biorefineries are classified into ten categories from L to V, and one of the categorised biorefineries (Q) uses green biomass [1], known as green biorefineries. Green biorefineries involve the sustainable processing of green biomass with a high content of organic compounds, such as legumes and grasses, that can be converted into marketable products [2,3].

Ensiling is commonly used as a preservation technique to ensure grass availability as a feedstock in a green biorefinery throughout the year. During ensiling, forages are kept under anaerobic conditions to quickly establish lactic fermentation, in which endogenous or additional lactic acid bacteria metabolise the water-soluble carbohydrates in the grass into different compounds that lower the pH of the system [4]. Fructose, glucose, mannitol, NaCl, KCl, $MgSO_4$, acetic acid, lactic acid, butyric acid, valeric acid and formic acid are some of the specific compounds of the grass silage [5].

The first step for a green biorefinery utilising grass is the mechanical fractionation of the clippings by screw pressing, during which green juice and a press cake are obtained. Grass silage juice, obtained after pressing the ensiled material, is a rich source of minerals, sugars, and organic acids [6]. From this complex mixture, lactic acid recovery and purification are the most studied due to its versatility, projected market value [7] and potential as a building block for the bioeconomy. However, there is no unique established procedure for lactic acid recovery.

Consequently, several downstream processes are carried out, like precipitation, solvent extraction, electrodialysis, adsorption, molecular distillation, esterification and membrane separation [8]. For the latter, microfiltration, ultrafiltration, and nanofiltration [9,10] are techniques being developed and constantly changing to purify lactic acid [11–13]. In this

process, the feedstock is fractionated through membrane separation into a retentate, where the high molecular weight components are retained, and a permeate, where low molecular weight components are contained [14]. Lactic acid is kept purer on the permeate side, while sugars, minerals and a fraction of organic acid are kept in the retentate [8,15]. One significant issue in the current proposed process is membrane fouling. Additionally, key parameters such as membrane selectivity and permeability are crucial. Achieving a high selectivity involves removing most impurities from a stream and enabling precise separation among different solutes [16]. Moreover, maintaining or enhancing high permeability, essential for efficient lactic acid, is critical [10].

Despite the vast literature on lactic acid separation through membranes, no related research has been found regarding the re-valorisation of secondary effluents in the membrane process. Generally, the retentate is not supplementary considered or reported for purposes other than biogas production. Nevertheless, the retentate is a side stream rich in molecules that can be valorised in a circular economy concept. Therefore, further studies are needed to evaluate the feasibility of recovering these streams. As an alternative application of the retentates, this research proposes to evaluate microalgae growth using all the streams produced in lactic acid recovery.

Taking into account that nutrients can account for up to 40% of the total production cost of microalgae [17], efforts have been made to grow and produce microalgae biomass in a multifunctional, sustainable and low-cost system to recover phosphorus, nitrogen and other nutrients from different effluents [18]. Due to the flexibility of microalgae development in various cultivation conditions (photoautotrophic, heterotrophic, photoheterotrophic, and mixotrophic), using effluents as a culture medium can be advantageous [19–21].

Only a few studies have been found about using grass (silage) juice for microalgae production. For instance, Xiu et al. [22] determined that the optimal concentration of Miscanthus press juice to grow *Chlorella vulgaris* was a culture medium that contained 15% of the juice concentration. Moreover, Rhaman et al. [23] cultivated *Chlorella* spp. with 10% cattail juice as a culture medium. Furthermore, Schoeters et al. [24] tested different fresh grass juice pretreatments to grow microalgae, obtaining successful growth at 10% juice concentration.

Thus, this study aimed to investigate lactic acid recovery from grass silage juice using membrane processes and the novel use of the secondary effluents produced in the downstream processing of lactic acid to grow *Chlorella vulgaris*.

2 Materials and methods

2.1 *Membrane separation experiments*

2.1.1 Feed solution

The initial stream used in the membrane process was grass silage juice (GSJ). To obtain GSJ, local farmers supplied grassland silage, which was then compressed using a standard agricultural procedure of screw press. Subsequently, GSJ underwent pre-filtration using a bag filter to remove the larger suspended particles. After this procedure, GSJ was transported to TU Wien, where it was kept frozen at -20 °C until further use. The composition of the grass silage is given in Table 1.

Table 1. Grass silage juice composition

Grass Silage Juice Composition [GSJ]			
pH	4.74	**Fe [ppm]**	30.622
Conductivity [mS/cm]	9.81	**Mn [ppm]**	6.63
TKN [ppm]	194.17	**Mg [ppm]**	132.20
Glucose [ppm]	5189.11	**Na [ppm]**	13.80
Fructose [ppm]	5054.49	**Ca [ppm]**	692.20
Succinic acid [ppm]	1111.64	**K [ppm]**	2576.30
Lactic acid [ppm]	5797.77	**Al [ppm]**	11.13
Acetic acid [ppm]	1262.09	**Cd [ppm]**	2.60
Pyroglutamic acid [ppm]	83.40	**Co [ppm]**	2.42
Ethanol [ppm]	164.55	**Cr [ppm]**	3.40
Propionic acid [ppm]	882.99	**Cu [ppm]**	1.64
P [ppm]	251.14	**Ni [ppm]**	2.3571
S [ppm]	40.02	**Zn [ppm]**	4.04

2.1.2 Cross-flow microfiltration and nanofiltration experiments

A membrane process was performed to purify lactic acid from GSJ, combining microfiltration (MF) and nanofiltration (NF). Microfiltration was carried out using a cross-flow-membrane module with an effective area of 0.008 m^2. A flat sheet MF membrane with a pore size of 0.1 µm (Alfa-Laval-MFG1) was installed in the membrane module. A piston pump (CAT-high pressure, model 231) recirculated the GSJ. The applied pressure was 3 bar at 25 °C. After three hours of MF, two streams were produced: a microfiltration retentate (MFR), which corresponded to 30% of the GSJ, and a microfiltration permeate (MFP), which corresponds to

70% of GSJ in terms of volume. Hypothetically, the MFR contained particles, microorganisms, and macromolecules, and the MFP contained organic acids, sugars and minerals. Afterwards, a nanofiltration process took place using the same equipment for MF but a different membrane with a molecular weight cut-off (MWCO) of 200-300 Da (NF245). The feedstock for the nanofiltration was MFP. The pressure for NF was 32 bar, and the temperature was 25 °C. The NF process resulted in two streams: a nanofiltration permeate (NFP), which is the 70 % of the initial volume and a nanofiltration retentate (NFR). Theoretically, NFR contained sugars, a fraction of organic acids and minerals, while NFP contained only organic acids and minerals. Lactic acid recovery was calculated according to Alvarado-Morales et al. [25].

2.2 *Microalgae Cultivation*

2.2.1 Initial microalgae inoculum

The microalgae *Chlorella vulgaris* was selected for the study and was initially kept in Bold's Basal Medium (BBM). The microalgae culture was maintained in 100 ml Erlenmeyer flasks containing 50 ml of BBM under non-sterile conditions. Flasks were continuously agitated at 100 RPM under room temperature. Cool-white florescent lights provided the illumination with an intensity of 80 to 90 µmol m^{-2} s^{-1} with a 16/8 light/dark cycle.

2.2.2 Microalgae cultivation conditions

Cultivation of microalgae was performed in 100 ml Erlenmeyer flask as experimental units. Each flask contained one of the five streams produced during the lactic acid purification: GSJ, MFR, MFP, NFR, and NFP. Additionally, BBM was used as a control condition. The five streams were initially diluted 10x with deionised water, and GSJ, and MFR were additionally diluted 20x. The diluted streams were then filtered in 0.2 µm filters, and the pH was adjusted to 8 with NaOH (1 N) to avoid microbial contamination of the microalgae cultures before the microalgae inoculation, following the results of Schoeters et al. [24].

Once the culture medium was adjusted, an inoculum of 2 x 10^6 cells ml^{-1} was added. The flaks were covered with a cotton cap. The experimental units were agitated at 100 RPM under room temperature with a 16/8 light/dark light cycle. All the experiments were carried out simultaneously in triplicates for five days.

2.3 *Analytical methods*

2.3.1 Streams chemical characterisation

GSJ, MFP, MFR, NFP and NFR were chemically characterised regarding organics, amino acids and sugars by HPLC by the Laboratory for Chemical Analysis at Ghent University. Nutrients and heavy metal content were determined by Inductive Coupled Plasma-Optical Emission Spectroscopy (ICP-OES, Varian Vista MPX, USA) after a hot-plate digestion, in which a mixture of 2.5 mL of sample culture medium, 2 mL HNO_3 and 1 mL H_2O_2 were heated until the colour was removed and sediments dissolved.

2.3.2 Determination of microalgal growth

The growth was monitored by cell counting using a Neubauer chamber by direct observation on a bright-field microscope. A 1 ml homogenised sample was taken from each experimental unit and diluted when necessary before counting. The sampling was conducted 24, 48, 72, 96 and 120 hours after the inoculation.

2.3.3 Chlorophyll content

The concentration of chlorophyll was measured at the end of each experiment. To extract the chlorophyll, 5 mg (previously manually milled with inert sand) of each microalgae sample was mixed with 5 mL of methanol (100%). The mixture was vortexed 12 times every five minutes for 20 seconds. After that, samples were centrifuged for 10 min at 10,000 RPM to collect the supernatant. The chlorophyll a (1) and chlorophyll b (2) content of *C. vulgaris* was quantified

using the supernatant by spectrophotometry at 652 and 665 nm. The chlorophyll a and b were calculated using the following equations [26]:

$$\text{Chl-}\alpha(\text{mg/g}) = \frac{(-8.0962 \times A_{652} + 16.5169 \times A_{665}) \times V}{\mathbf{1000} \times W} \quad (1)$$

$$\text{Chl-}\beta(\text{mg/g}) = \frac{(\mathbf{27.4405} \times \mathbf{A_{652}} - \mathbf{12.1688} \times \mathbf{A_{665}}) \times \mathbf{V}}{\mathbf{1000} \times W} \quad (2)$$

V =Volume (ml); W =Weight of the sample (g); A_{652} = wavelength at 652 nm; A_{665} = wavelength at 665 nm.

The total chlorophyll was calculated by adding Chl-α and Chl-β.

3 Results and discussion

3.1 *Membrane performance*

Grass silage juice (GSJ) is a complex combination of chemical compounds; therefore, separating valuable products is a high-tech challenge. The optimal configuration of an integrated membrane process using MF and NF can improve the extraction and purification of target compounds. The most common membrane configuration includes using membranes from higher to lower MWCO according to the molecular weight of the recovered compound [15]. Microfiltration is essential to remove macroparticles and microorganisms that might be contained in the grass silage, and it is a crucial step to prevent further fermentation during downstream processing. The rejection of organic acids and sugars from the grass silage to the permeate is low for microfiltration, around 5 to 10% of each compound (Section 3.1.2). The critical purification process is nanofiltration, which will be discussed in the following sections.

3.1.1 Evaluation of lactic acid recovery

A completely clear broth was obtained after MF and NF (NFP). A stream of 1.5 g L^{-1} of lactic acid was obtained in the NFP, recovering only 25.86% concerning GSJ, which demonstrates a poor performance of the process. In addition, NFP was not highly purified in terms of lactic

199 acid due to the presence of acetic acid, succinic acid, ethanol, and propionic acid (**Error!**
200 **Reference source not found.**).

201 The poor performance in NF is probably due to GSJ having a pH of 4.74. The influence of the
202 pH solution directly affects the dissociation of lactic acid, meaning that 90% of LA is
203 dissociated at pH 4.74, and the isoelectric point of the membrane is also negative at that pH.
204 Hence, the Donnan exclusion effect plays a role in this separation [27]. An optimisation of pH
205 may result in better performance of the separation given that the pKa of lactic acid is 3.86.
206 Lowering the pH below the isoelectric point will result in an undissociated lactic acid molecule
207 and, consequently, neutrally charged. The charge neutrality of lactic acid facilitates the
208 permeation of the molecule through the membrane. In addition, further steps like monopolar
209 electrodialysis, bipolar electrodialysis, cation exchange, anion exchange and vacuum
210 evaporation are needed to obtain a pure lactic acid solution [28–30].

211 Table 2. Composition and concentration in ppm of MFR, MFP, NFR and NFP

Compound	MFR	MFP	NFR	NFP
Glucose	6099.12	5166.60	6256.46	137.06
Fructose	6256.61	5318.47	6469.56	111.64
Succinic acid	1414.17	1214.02	1396.90	381.31
Lactic acid	6875.96	5972.71	6518.94	1460.30
Acetic acid	1446.06	1299.89	1009.07	848.62
Pyroglutamic acid	106.14	87.08	102.59	3.98
Ethanol	240.64	158.94	97.41	104.19
Propionic acid	1108.41	932.70	923.57	391.60
P	465.03	133.40	491.705	32.261
S	77.42	20.87	69.02	5.42
Mg	254.06	67.34	272.40	0.72
Na	16.69	16.13	18.01	16.13
N	272.96	171.65	230.75	84.42
Ca	1173.15	359.13	1228.60	1.69
K	n.d	1128.30	n.d	734.07
Al	15.68	6.78	9.80	6.42

Cd	2.77	2.76	2.66	2.48
Co	2.30	2.25	2.84	2.63
Cr	3.55	3.28	3.48	3.27
Cu	2.15	1.57	1.94	1.76
Fe	74.09	6.42	18.05	3.07
Mn	9.47	4.40	9.66	2.96
Ni	2.11	1.60	2.65	2.66
Pb	5.78	6.30	9.36	5.47
Zn	6.63	2.37	7.34	1.04

* n.d.: non-detected.

In order to better understand the process for a future optimization, the rejection of the main components in GSJ was calculated for both MF and NF steps and the results are presented and discussed below.

3.1.2 Organic acids and sugars fractionation during the multistage process

The primary process for microfiltration is to remove macroparticles, macromolecules and microorganisms that might be contained in the grass silage. Figure 1 shows the organic acid and sugar contents in every stream during NF and MF.

The MF step was successful as it allowed for most of the molecules to pass while reducing the presence of particles and colour in the MFP. The rejection of fructose and glucose was 5.96% and 8.46 %, respectively. Although the molecular weight of fructose and glucose is the same (180.156 g mol^{-1}), the slightly different rejection might be influenced by the structure of both molecules. Regarding organic acids, the rejection was also low, with 3.87%, 5.75%, 4.00%, 8.12% and 6.33% for succinic acid, lactic acid, acetic acid, pyroglutamic acid, and propionic acid, respectively. The low rejection of organic acids in MF is an advantage because almost 90% of the initial concentration (GSJ) is retained in MFP, which is the feed for NF.

The highest overall rejection was for glucose, fructose, and pyroglutamic acid, with 98.71, 98.92, and 97.66%, respectively, when combining both membrane separation methods. The multistage process improved fructose and glucose rejection compared to Wang et al. [31], who

found a 2.55% glucose and 4.49% fructose of rejection. Even though the membrane used in their study was NF270, which has a similar MWCO to the NF245 used in this study, the operating condition regarding pressure was different. Moreover, NF245 was reported to retain more than 52% organic material and 23% salt [32]; however, for glucose, fructose, citric acid, and pyroglutamic acid compounds, the retention was nearly 100% in our study.

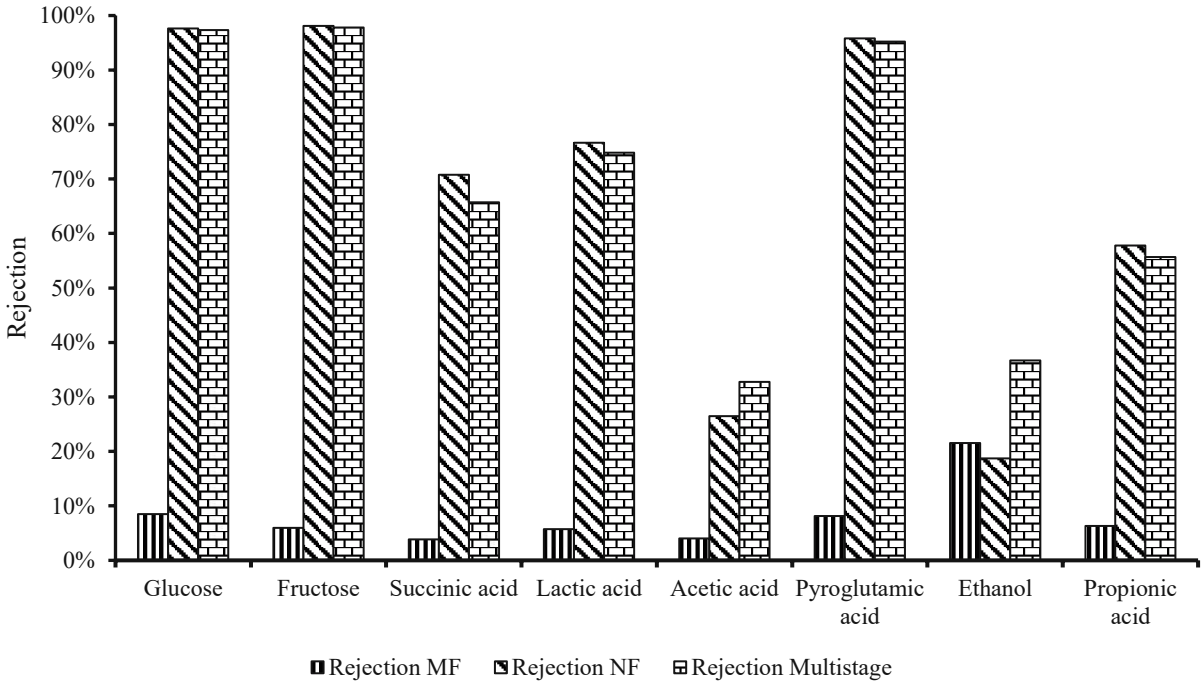

Figure 1. Rejection of organic acids and sugars during microfiltration, nanofiltration and multistage process. GSJ: Grass Silage Juice, MFR: Microfiltration Retentate, MFP: Microfiltration Permeate, NFR: Nanofiltration Retentate and NFP: Nanofiltration Permeate.

Using a multistage membrane configuration for organic compounds and sugar rejection plays an essential role in the purification of a desired compound. The compounds with a molecular weight heavier than the MWCO of NF245 were rejected by over 97 %, which is higher than the values found by Choi et al. [33].

Notably, both MFR and NFR are streams rich in fructose and glucose; therefore, both can be named secondary effluents due to the definition by Platt et al. [1] that secondary effluents or secondary biomass are a side-product or residue from primary biomass's conversion, process or decomposition.

3.1.3 *Desalination process and heavy metals rejection*

Membranes can partially or entirely remove heavy metals due to the Donnan exclusion effect, steric hindrance or size exclusion mechanism, and the adsorptive capability for specific contaminants [34]. NF is an ideal process for removing polyvalent cations, anions, suspended particles, and uncharged compounds [35]. Metals like chromium, zinc, lead, copper and nickel are toxic to human health, microorganisms, and the environment [36]. The rejection of heavy metals is shown in Figure 2.

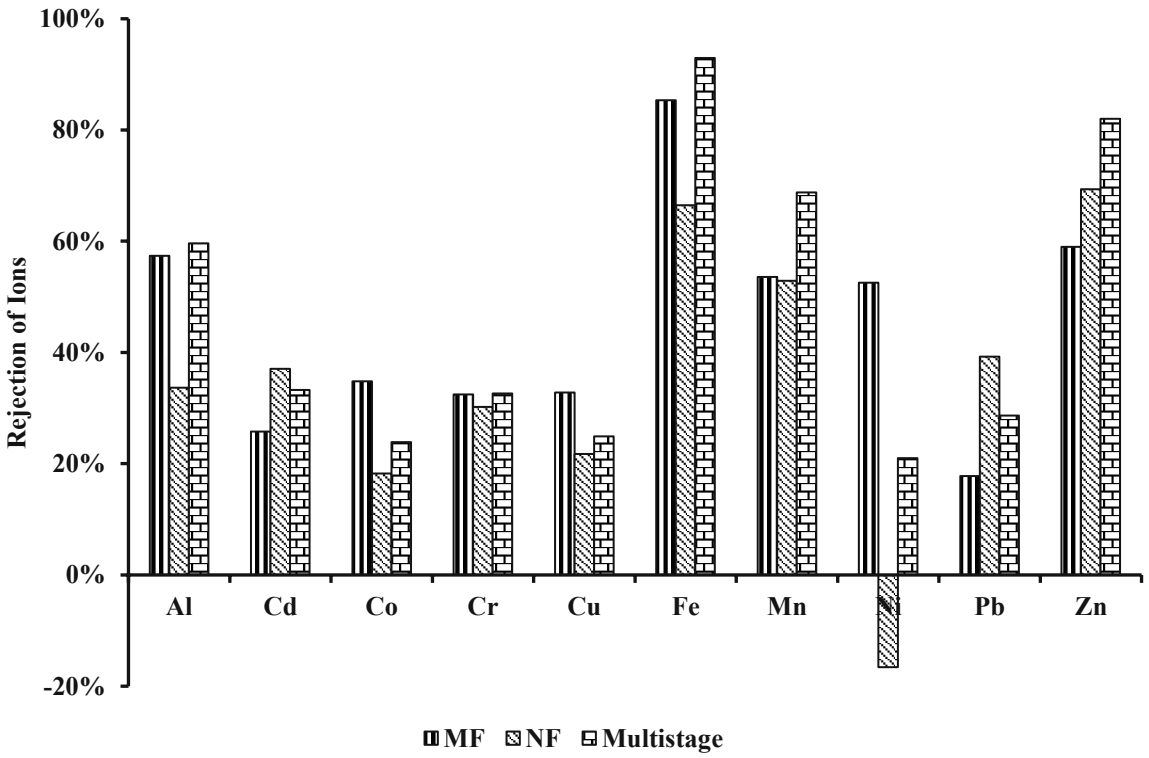

Figure 2. Rejection of heavy metals during microfiltration, nanofiltration and multistage process. GSJ: Grass Silage Juice, MFR: Microfiltration Retentate, MFP: Microfiltration Permeate, NFR: Nanofiltration Retentate and NFP: Nanofiltration Permeate.

The highest ion rejection was reached after NF for iron, manganese, and zinc, with 66%, 53%, and 69% rejection, respectively. Nickel presented negative rejection for NF (approx. -17%), which means that nickel permeated through the membrane, reaching a final concentration higher than the feed [37]. Nevertheless, the combination of MF and NF lead to a rejection of

21% for nickel. Regarding cadmium, cobalt, chromium, copper, and lead, the rejection rate for all those heavy metals was less than 40% for MF and NF. The use of thin film composite membranes has shown potential for treating GSJ and removing heavy metals. The steric hindrance mechanism mainly governs the rejection of metal ions. Several authors have reported higher rejection of iron, manganese and zinc, reaching 99.99 % when modifying the membrane surface with curcumin boehmite nanoparticles [38] or assembling the membrane with phytic acid [39].

3.2 *Microalgae cultivation*

Even though proper lactic acid recovery was not achieved with the proposed membrane process, streams with different compositions were obtained and the performance of microalgae cultivation under such conditions can help to guide future efforts to valorize such side-streams once the process has been optimized for lactic acid recovery. Therefore, the five streams obtained in this study were used for the cultivation of *C.* vulgaris and the results are shown in Figure 3.

The cultivation conditions significantly influence microalgae growth characteristics; mixotrophic conditions were achieved in this case, as all used streams had organic carbon (Table 1 and **Error! Reference source not found.**) in their composition [40]. The mixotrophic conditions improved the initial growth rate compared with the BBM medium for the five different culture media tested (Figure 3). However, for most of the tested media, the final cell count was similar to the one obtained in the control BBM medium. Only NFP performed slightly better than BBM, while GSJ resulted in cell death after the second day of growth.

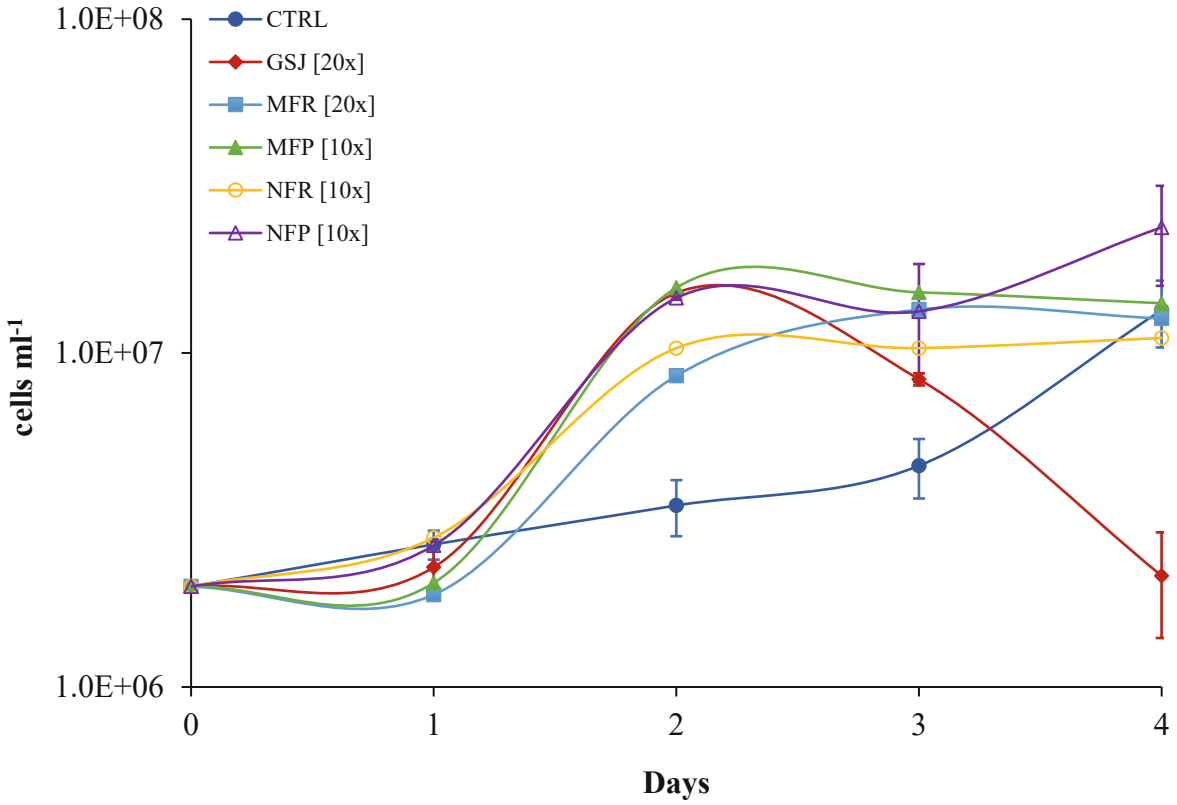

Figure 3. *Chlorella vulgaris* growth curve

Despite the high growth rates achieved, the disadvantage of mixotrophic cultivation is the potential microbiological contamination. Microalgae cultivated in MFR and NFP were quickly biologically contaminated after the second day of cultivation. For GSJ, the contamination was so intense that it resulted in cell death after the second day of cultivation. Therefore, sterile conditions or a fed-batch approach to keep the organic sugar concentration low in the growth medium might be needed to utilise these stream for microalgae cultivation. Moreover, the potential for interaction with algae-fungi or algae-bacteria [41] may open a new area of research for using retentates of MF or NF from grass silage.

Their chlorophyll content was determined to assess further the health of the cells grown on the different tested streams (Figure 4). After five days of cultivation, cells grown on NFP [10x] showed the highest total chlorophyll content (8.24 ± 0.34 mg g-1). This corresponded to an increase of 92% in total chlorophyll compared to the control group. On the contrary, the

minimum chlorophyll content was attributed to GSJ [20x] culture medium (0.66 ± 0.06 mg g^{-1}), which is 84% lower chlorophyll production than the control.

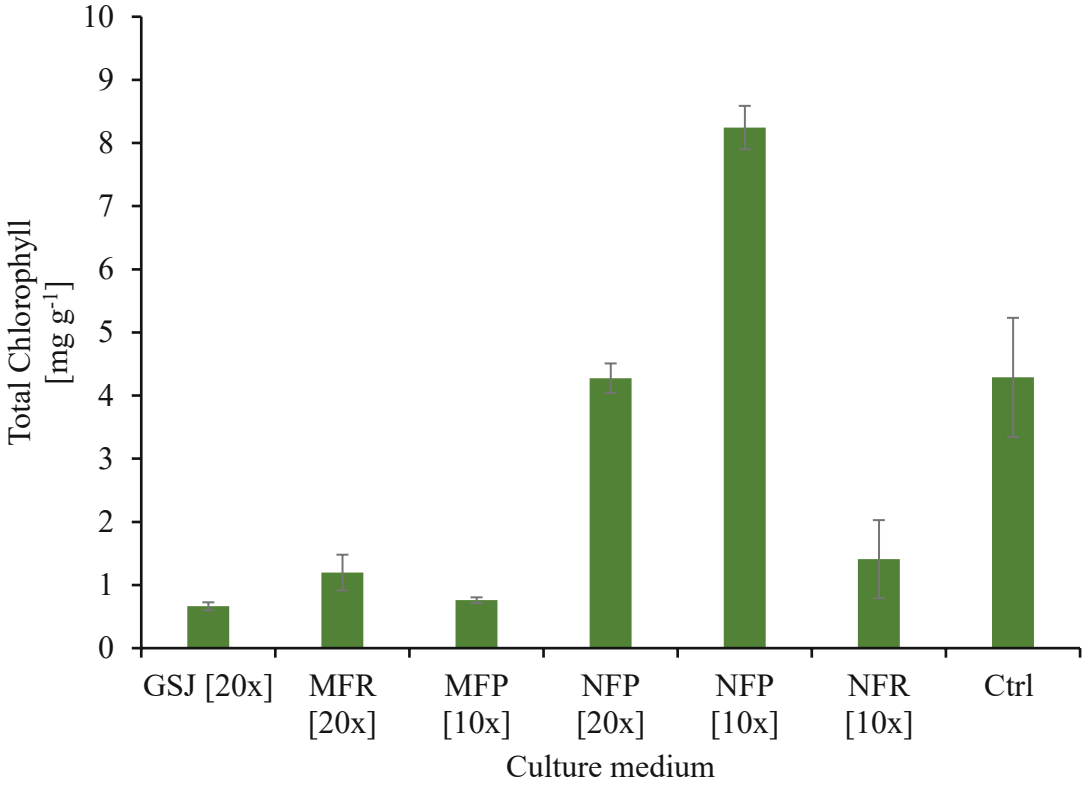

Figure 4. Total chlorophyll content of *C. vulgaris* in each culture medium after five days of growth

In mixotrophic conditions, the concentration of glucose (6.0 g l^{-1} in all the mentioned streams, except NFP) inhibits the synthesis of chlorophylls [42,43]. Therefore, this phenomenon can be attributed to the low production of chlorophyll in most of the studied streams.

In NFP, lactic and acetic acids were the most concentrated compounds, present at 1.5 g L^{-1} and 0.8 g L^{-1}, respectively. Acetic acid has been reported as a carbon source for microalgae culture. For instance, Bo et al. [44] demonstrated significant growth of *Chlorella* sp. in acetic acid, which was suggested to be a promoter for the mixotrophic condition of *Chlorella* sp. compared to the autotrophic growth conditions. Furthermore, Li et al. [45] reported the heterotrophic and

mixotrophic cultivation of the microalgae *Chlorella pyrenoidosa* using acetic acid as a carbon source.

On the other hand, Turon et al. [46] characterised the growth of *Auxenochlorella protothecoides* and *Chlorella sorokiniana* in the presence of lactate, butyrate, and acetate. The authors found that the microalgae was not able to assimilate lactate. Consequently, this limitation could be advantageous for proposing future purification processes using microalgae,as they could potentially consume the other compounds while resulting in a lactic acid stream with higher purity. This gap presents an opportunity to explore the potential of microalgae cultivation as a novel method for lactic acid purification, which could offer a sustainable and efficient solution.

4 Conclusions

Our results showed that using microfiltration followed by nanofiltration partially purified lactic acid from grass silage juice; however, the acidic pH of this stream resulted in low recovery in the end stream. Moreover, the proposed lactic acid recovery process would need extra purification steps to achieve better results, as it was not possible to obtain a rich and pure stream of lactic acid after membrane separation. An innovative approach utilising grass silage juice and secondary effluents from the lactic acid production process was also tested and offered significant potential for sustainable and cost-effective microalgae cultivation. Interestingly, the stream with the highest lactic acid concentration (nanofiltration permeate) promoted the best microalgae growth and chlorophyll content. This result can open the possibility of using microalgae as a further step in the purification of lactic acid, as *Chlorella* is not known to use lactic acid and would, therefore, use the other molecules, potentially yielding a purer lactic acid stream after cultivation.

CRediT Authorship contribution statement

Mayuki Cabrera-González: Conceptualization, methodology, Formal Analysis, Investigation, Data Curation, Writing – Original Draft. **Marcella Fernandes de Souza** Conceptualization, methodology, Formal Analysis, Investigation, Writing – Review and Editing, Supervision. **Erik Meers**: Review, Supervision, Project administration, Funding Acquisition. **Amal Ahmed**: Experimental Setup (membranes), supervision, and Review. **Michael Harasek**: Review, Supervision, Project administration, Funding Acquisition.

Declaration of Competing Interest

Declaration of interest: none

Data Availability

Data will be made available on request.

Acknowledgements

This work was supported by the European Union's Horizon 2020 – Marie Skłodowska-Curie research and innovation program (Grant agreement No 860477) as part of the AgRefine project. We thank Marie-Chantal Heerteler for supporting the chemical analyses and microalgae cultivation.

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EXPERIENCE

Project Assistant — 09/2020 - 09/2023

Technische Universität Wien — Vienna, Austria

- Development and optimisation of the downstream processing of lactic acid from waste streams through micro and nanofiltration membranes and electrodialysis
- Presenting at scientific events (conferences, workshops, and seminars) and writing scientific publications in international journals (https://shorturl.at/FIKW9)
- Participation in research and projects related to sustainability, purification through membrane processes from fermentation processes, and utilisation of waste and effluents for biomass production
- Supervision of students (Bachelor's and Master's theses) and co-teaching
- Two Visitor Research Internships:

Visitor Researcher — 05/2022 - 07/2022

Gent University — Ghent, Belgium

- Improving microalgae biomass production with waste streams as a growth medium
- Analytics performance: ICP, refractometer, spectrophotometer, microscopy, cell counting, and Kjendahl Analysis
- Presenting at scientific events

Visitor Researcher — 01/2022 - 04/2022

University College Dublin — Dublin, Ireland

- Use and testing of GMO (*E. coli*) for biosensing to identify organic compounds in waste streams.
- Preparing culture medium and ensuring sterilisation
- PCR and microorganisms cultivation in liquid and solid medium.

Secondary School Teacher — 03/2016 - 09/2020

Colegio Eben Ezer — Antofagasta, Chile

- Instruct students aged 14 to 18 in math, chemistry, physics, thermodynamics, and mechanics.
- Served as a former tutor for the final school year, providing guidance and support to students.
- Led the Academy of Science, involving students in local and national conferences and competitions.

Research Assistant — 04/2014 - 12/2015

Universidad de Antofagasta — Antofagasta, Chile

- Conducted research focused on purifying lithium brines to obtain high-quality LiCl and LiOH for Li^+ batteries.
- Employed electrodialysis techniques to achieve efficient purification processes
- Research Assistant Universidad de Antofagasta, Antofagasta, Chile
- Performing potentiodynamic sweeps to determine the limiting current density of the reactions

S

I am a highly responsible,dedicated, motivated, proactive and goal-oriented professional with a genuine passion for continuous learning and collaboration. My extensive experience, spanning over adecade, includes research such as membrane technologies, microalgae, the food industry, biosensors, and molecular biology. In addition to laboratory work and teaching, it has equipped me with a wide range of practical knowledge and expertise. I excel internationally, using my strong communication skills to work effectively with diverse teams and obtain successful publicationresults.

LANGUAGES

Spanish	Native	●●●●●
English	Proficient	●●●●◆
German	Advanced	●●●◆◆

CERTIFICATIONS

Educational Project Management

Educational Assessment

Curriculum Design and Innovation.

Driving licence Type B

VOLUNTEERING

Caritas – Le⁺O

SAVT – StudentInnen und AbsolventInnen der Verfahrenstechnik and der Technische Universität Wien.

FemChem – TU Wien

EXPERIENCE

Junior Researcher
10/2012 - 01/2014

University of Chemical and Technology, Prague. Prague, Czechia

- Investigation of the utilisation of microalgae for anaerobic digestion under mesophilic and thermophilic conditions
- DNA extraction of microorganisms for further molecular biology analysis (PCR, Real-Time PCR)
- Proficiency in gas chromatography
- ***Fully funded by the Marie Skłodowska-Curie International Research Staff Exchange Scheme ALGAENET grant agreement No 295165***

Quality Control Analyst in Beverage Production
03/2011 - 10/2012

PepsiCo Antofagasta, Chile

- Conducted microbiological and physical-chemical analysis for soft drinks
- Proficiency in refractometer, titration, and microbiology

EDUCATION

Doctoral Programme in Engineering science in process and chemical engineering (Dr. Tech)
10/2020 - 06/2024

Technische Universität Wien Vienna, Austria

- Thesis: Downstream processing of lactic acid from grass silage juice using membrane
- Specialisation: Membrane processes
- ***Fully funded by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 860477***

Master of Education (MA)
03/2020 - 01/2022

Universidad Andrés Bello Santiago, Chile

- Thesis: Proposal for improving the practices of the school integration programme in third and fourth-grade pupils of the schools attached to it through the monitoring and quantifying of the progress of 21st-century skills
- Specialisation: Master in curriculum development and educational projects
- Master of Education ***(graduation summa cum laude)***

Master of Science (MSc)
03/2016 - 12/2018

Universidad de Antofagasta Antofagasta, Chile

- Thesis: Lithium recovery from lithium brines through electrodialysis to be used as a lithium-type
- Specialisation: Engineering science, mention mineral processing and process engineering
- Master of Science ***(graduation summa cum laude)***

Biotechnology (BSc)
01/2007 - 12/2011

Universidad de Antofagasta Antofagasta, Chile

- Biotechnology (5-year HONS degree) ***(graduation summa cum laude)***
- Thesis: Microalgae pre-treatment for anaerobic digestion in thermo and mesophilic conditions.

PUBLICATIONS

- Papadopoulou E. and Cabrera-Gonzalez M., et al. (2023). Membrane separation of lactic acid from fermentation broth produced by organic residues. Journal of Environmental Chemical Engineering 11 (5), 110881
- Cabrera-Gonzalez M., et al. (2022). Development of a model for the implementation of the circular economy in desert coastal regions. Land 11 (9), 1506.
- Cabrera-Gonzalez M., et al. (2022). Evaluation of nanofiltration membranes for pure lactic acid permeability. Membrane 12 (3), 302.

SKILLS

- Quantitative and qualitative chemical analysis (HPLC, ICP, GC)
- Membrane Technologies
- Supervision and mentoring
- Teaching
- Data Analysis
- Microbiology
- Molecular biology
- MS Office
- Writing scientific articles