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Expanding the applicability of reactive distillation

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- Pazmiño-Mayorga, I.P., Kiss, A.A., Jobson, M., 2021. Novel Dual Reactive Distillation Process for Eco-efficient Lactic Acid Recovery and Purification from Fermentation Broth, in: Türkay, M., Gani, R. (Eds.), Computer Aided Chemical Engineering, 31 European Symposium on Computer Aided Process Engineering. Elsevier, pp. 57–62.
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Abstract

Development and innovation of sustainable technologies are critical for the clean and efficient production of chemicals and biochemicals. Reactive distillation (RD), a successful example of Process Intensification (PI), offers environmental and economic advantages compared to conventional technologies and contributes to sustainable development by combining reaction and separation. This synergistic combination allows overcoming azeotropes while increasing reaction rates, overcoming chemical equilibrium, and improving selectivity. The main advantages of RD include reduced footprint due to integrated functions in a single device that results in energy savings (e.g., the heat of reaction is used to assist vaporising the liquid phase), increased safety due to reduced inventories and the ability to avoid runaway reactions. However, the applicability of RD – the fact of being useful in a particular application – is limited because the operating conditions for reaction and separation need to overlap.

Advanced reactive distillation technologies (ARDT) integrate the benefits of RD and additional features of PI, allowing greater overlap between reaction and separation operating conditions, which are represented and evaluated in operating windows. Therefore, this PhD thesis focuses on expanding the applicability of reactive distillation into typically restricted chemical systems and operating conditions by enabling rapid and early-stage systematic assessment of the technical feasibility of ARDT using first principles and heuristics. The technologies studied in this research are reactive dividing-wall columns (R-DWC), catalytic cyclic distillation (CCD), reactive internally heat-integrated distillation (R-HIDiC), reactive high-gravity distillation (R-HiGee), and membrane-assisted reactive distillation (MA-RD). These technologies have demonstrated better performance than conventional configurations in simulation-based studies. However, their industrial application is still scarce.

To date, the synthesis and design of chemical processes progressively rely on complex computational methods thanks to the increase in computing power and the development of more robust solvers. Most of these approaches cover a range of traditional and well-established unit operations, while intensified equipment is considered superficially, especially novel technologies such as advanced reactive distillation. Process synthesis, targeting intensified equipment, will help process designers develop novel process flowsheets applying non-conventional processing options, where these can improve process performance by reducing energy consumption, increasing throughput, and reducing waste with a safer operation. This research is the first to create and provide a systematic approach targeting ARDT to expand the applicability of reactive distillation.

This PhD thesis aims to develop a systematic methodology to expand the applicability of reactive distillation by assessing the technical feasibility of advanced reactive distillation technologies during process synthesis, while minimising requirements for process data and computational effort. Published case studies covering experimental, modelling, simulation and optimisation investigations and a study within the thesis – conceptual design of a dual reactive-dividing wall column using rigorous models in Aspen Plus – are used to underpin the research approach, the development of the methodology and the testing and verification of the resulting flowsheets.

The basis and scope of the methodology to be developed was established in a conceptual framework that considers key thermodynamic properties and kinetic parameters for a given chemical system and its liquid-phase reactions and by formulating high-level questions. Furthermore, the simultaneous reaction and separation result in complex mixtures containing components in varying amounts and of different natures (e.g., reactive, inert), which can affect operation by narrowing operating windows. To represent and identify potential interactions between the components of the system and the operating conditions, this thesis develops and introduces new concepts (representative components and sliding windows) for the development of operating windows. These new concepts aim to facilitate the analysis and identification of the pressure ranges suitable for ARDT, sometimes expanding the range of conditions, relative to conventional reactive distillation.

The high-level questions are organised in the synthesis methodology in four categories represented in a decision-making flowchart. This flowchart provides yes/no answers and interpretation of numerical values that categorise each technology qualitatively as advantageous, technically feasible or not applicable. The synthesis methodology also supports the selection of a particular advanced reactive distillation technology with first principles that have a sound theoretical basis and heuristics based on empirical generalisation derived from observations.

Additional industrially relevant case studies are used to demonstrate the application of the newly developed synthesis methodology. The predictions of the flowchart are verified in the light of quantitative evaluations carried out in published studies spanning different chemical systems and conditions, to provide confidence in the validity of the results. The flowchart suggests which of the ARDT merit further investigation and the range of suitable operating conditions that can be used to develop detailed designs. In this manner, resources for more detailed design tasks can be applied efficiently while widening the design scope to include ARDT with less computational effort during flowsheet development.

The synthesis methodology supports screening and identification of potentially advantageous process concepts. However, its application is limited to early-stage evaluation as interactions arising from complex reaction networks, feeds of variable composition and properties of the chemical system that depend on compositions and operating conditions need to be assessed with detailed investigations. Contradicting technology suggestions could occur, which cannot be attributed to a single selection criterion, and a trade-off evaluation may be necessary. In addition, the synthesis methodology does not support the evaluation of the process economics to allow alternative process configurations to be compared quantitatively. Further research to develop models to assess process performance and economics quantitatively is highly encouraged to enable a fair comparison between conventional and novel technologies.

Declaration of originality

I hereby confirm that no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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Dedication

To my mom, Celina Beatriz Mayorga Pérez

I started this PhD with your blessing when we said goodbye at the airport in March 2019. I never thought I would be celebrating this achievement without you. You gave me light and love for almost 35 years. Despite the adversities due to health issues, our lives were enjoyable. You had the strength and positive attitude that inspired us all.

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Your daughter,

Isabel Cristina

A mi madre, Celina Beatriz Mayorga Pérez

Comencé este doctorado con tu bendición cuando nos despedimos en el aeropuerto en marzo de 2019. Nunca pensé que estaría celebrando este logro sin ti. Me diste luz y amor durante casi 35 años. A pesar de las adversidades por problemas de salud, nuestras vidas eran agradables. Tuviste la fuerza y la actitud positiva que nos inspiró a todos.

Estoy agradecida de haber tenido la oportunidad de compartir viajes y recuerdos hermosos contigo, para que podamos recuperar algunos de esos momentos perdidos cuando tuviste que estar en el hospital luchando contra la enfermedad cuando yo era solo una recién nacida y en los primeros años de mi infancia. Y luego, durante tus últimos días en este mundo, estuvimos luchando a tu lado en el hospital, en casa y en el hospicio.

Siempre fuiste sabia. Me doy cuenta de lo mucho que aprendí de ti a lo largo de mi vida en cada acción. Gracias por tus enseñanzas y palabras de aliento. Gracias por esas veces que me escuchaste en silencio, reflejando mis lágrimas, y tu empatía fue suficiente para darme paz. Fue tan difícil verte partir. Te sigo extrañando, siempre.

Tu hija,

Isabel Cristina

The author

Isabel Cristina Pazmiño Mayorga was born in Quito, Ecuador and obtained her BSc in Chemical Engineering at the Escuela Politecnica Nacional in Quito in 2012. She also holds an MSc in Advanced Chemical Engineering from the University of Manchester, awarded in 2015 with Distinction. She started her PhD studies at the Centre for Process Integration at the University of Manchester in 2019. Her research focused on expanding the applicability of reactive distillation by applying process intensification and process simulation to develop a methodology for the synthesis of novel process flowsheets.

Isabel has three years of industrial experience in oil refining, cement manufacturing and gold extraction. Isabel also held academic positions in Ecuador, as a lecturer for over three years, and in the United Kingdom, as a Graduate Teaching Assistant during her PhD studies. Isabel has a special interest in foreign languages and communication.

Isabel is about to start a Research Associate position at the Department of Chemical Engineering at the University of Manchester, researching process integration and decarbonisation of energy-intensive processes.

Chapter 1

Introduction

1.1 Introduction and background

This PhD thesis is driven by the need for sustainable chemical processes applying innovative technologies. These technologies can offer benefits, such as increasing the efficiency with which material and energy resources are used. They can also reduce capital expenditure and plant footprint while reaching the desired product specifications and improving performance. These benefits can be realised through process intensification (PI) (Harmsen and Verkerk, 2020).

Process intensification is an emerging field in chemical engineering that seeks to improve a chemical process by orders of magnitude in terms of economics, environmental and safety performance by increasing energy efficiency, reducing waste generation and plant footprint, potentially leading to reduced costs (Stankiewicz and Moulijn, 2000; Tian et al., 2018). The means to achieve an intensified processing system include (Stankiewicz et al., 2019):

- Reactions at maximum achievable efficiency
- Uniform processing history for all molecules
- Removal of hydrodynamic, heat and mass transfer limitations
- Maximise the synergies resulting from interrelations between various operations and steps

These ideas are captured in the generic principles of process intensification and the four domains of process intensification (detailed in the Literature Review) proposed by Van Gerven and Stankiewicz (2009). Figure 1.1 summarises this approach to understanding process intensification, including examples of intensified methods, equipment and materials, along with the scales at which they have an effect.

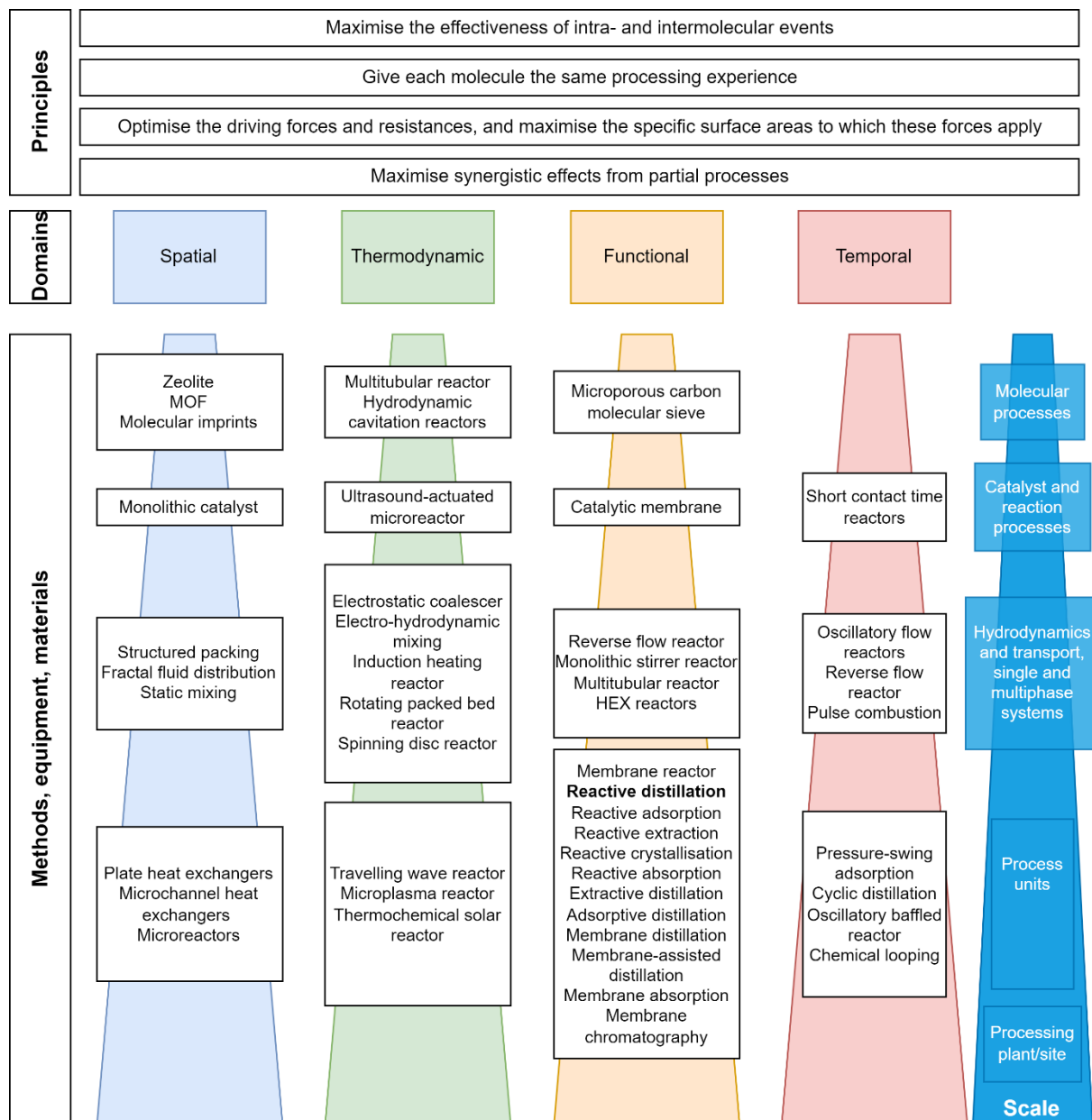


Figure 1.1. Principles, domains, methods, equipment and materials of process intensification (adapted from Stankiewicz et al. (2019))

An example of process intensification is reactive distillation, which combines reaction in the liquid phase and separation in the vapour phase in a single unit. This configuration presents benefits compared to a traditional flowsheet with a reactor-distillation-recycle structure (Figure 1.2). Since the chemical equilibrium is overcome due to the constant removal of the reaction products, it results in improved conversion and yield, less recycling and a reduced number of devices (Kiss, 2013; Orjuela et al., 2016). Despite the numerous advantages of reactive distillation, limitations hinder its widespread use, such as the need for an overlap in the operating pressures and temperatures to enable simultaneous reaction and separation (Luyben, 2013; Seader, 2011).

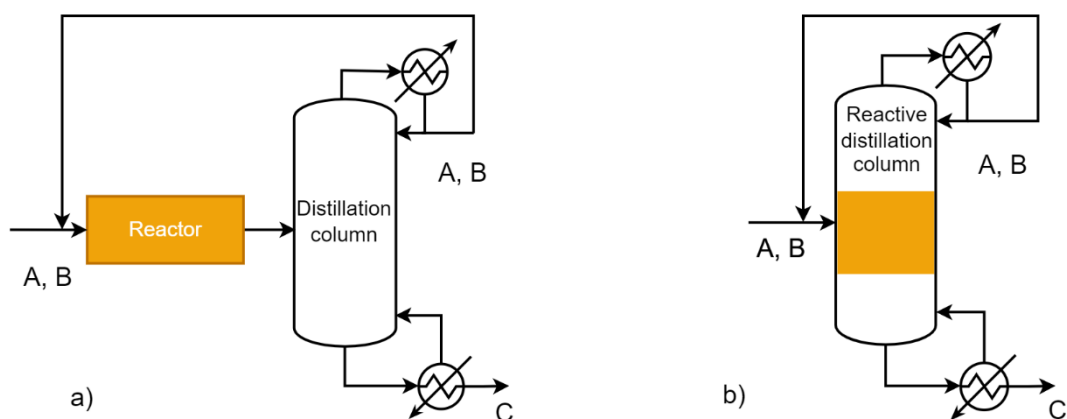


Figure 1.2. a) Conventional reactor-distillation-recycle structure, b) reactive distillation column

Recent experimental and modelling-based research has explored introducing additional intensification features to reactive distillation columns. These new features lead to new configurations – advanced reactive distillation technologies (ARDT), namely:

- a dividing wall in a reactive dividing-wall column (R-DWC)
- introducing a dynamic state in the operation by manipulating the duration of an event in catalytic cyclic distillation (CCD)
- internal heat integration and vapour recompression in reactive internally heat-integrated distillation (R-HIDiC)
- use of centrifugal/centripetal force in reactive high-gravity distillation (R-HiGee)
- a membrane to aid separation in membrane-assisted reactive distillation (MA-RD).

Advanced reactive distillation technologies have the potential to expand the applicability of reactive distillation and overcome some of its limitations, which are discussed in more detail in the literature review. For example, it is possible to expand the range of applications in terms of operating conditions or the type of chemical systems that can be used, which can offer alternative processing options that are potentially more efficient. However, current chemical process design practice focuses on conventional unit operations that have been optimised for many years, while intensified units still require significant investments in capital, time and resources (Boffito and Fernandez Rivas, 2020).

Intensified units present a high degree of complexity, which makes process synthesis and design challenging due to the simultaneous occurrence of multiple phenomena. This complexity is particularly problematic for the design of advanced reactive distillation technologies because their additional intensification features are not adequately reflected in existing models and simulation tools, which in turn complicates the synthesis of processes

(Kiss and Smith, 2020). Currently, methodologies for the design of advanced reactive distillation technologies rely on standalone technology-oriented procedures (i.e., developed for a particular application using a predetermined technology) rather than taking a holistic view of the process flowsheet. These methodologies for synthesis and design will be discussed in more detail in the literature review.

Incorporating intensified units in chemical process design can produce more sustainable solutions than conventional flowsheets that could be exploited in industrial applications (Tula et al., 2020). As a result, significant improvements, in terms of operational, economic, regulatory and environmental performance, could result (Orjuela et al., 2016; Stankiewicz et al., 2019). At the same time, additional intensification applied to reactive distillation can contribute to making chemical processing cleaner, more energy-efficient, and substantially smaller, which aligns with contributing to reaching the United Nations Sustainable Development Goals (SDG) related to increasing energy efficiency (SDG7); upgrading infrastructure and retrofitting industries to make them sustainable using cleaner technologies (SDG9); and reducing waste generation, sustainable management, and efficient use of natural resources (SDG12) (Harmsen and Verkerk, 2020; United Nations, 2015).

To date, the advanced reactive distillation technologies investigated in this PhD thesis have not been included in synthesis and design methodologies reported in the research literature. This thesis proposes expanding the applicability of reactive distillation, by incorporating further intensification, to overcome its limitations in terms of operating conditions or the type of chemical systems that can be applied, resulting in more efficient operation. Using first principles and heuristics in the early stage of process synthesis, the proposed approach offers a methodology to assess simultaneously the technical feasibility of five advanced reactive distillation technologies by providing insights on their advantages and disadvantages in a decision-making matrix that facilitates visualising trade-offs with less computational effort than mathematical programming-based approaches.

1.1.1 Advanced reactive distillation: An example of process intensification

To incorporate process intensification during chemical process design, Van Gerven and Stankiewicz (2009) proposed a framework for evaluating simultaneous and multi-scale phenomena across four domains: functional, thermodynamic, temporal, and spatial.

The combination of reaction and separation functions in a reactive distillation unit is an example of the functional domain. The reaction improves the separation by overcoming

azeotropes, and the separation improves the reaction by enhancing reaction rates due to the continuous removal of the reaction products (Kiss, 2017; Sundmacher and Kienle, 2003). Nevertheless, these improvements are limited to an operating region where the reaction and separation can occur simultaneously. That is, the temperature and pressure conditions for the reaction and the separation must coincide (Kiss et al., 2019; Schembecker and Tlatlik, 2003). This requirement can be represented using a pressure vs temperature diagram, an ‘operating window’ that indicates conditions facilitating simultaneous reaction and separation (Figure 1.3). Additionally, unfavourable volatilities of the reactants and products and undesired side reactions must be addressed (Keller, 2014; Orjuela et al., 2016).

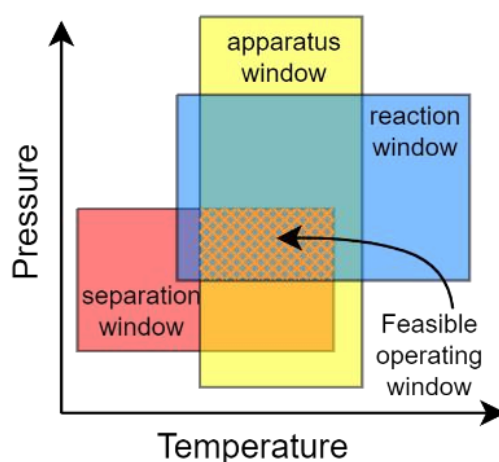


Figure 1.3. Overlapping windows to find the feasible operating window

This work proposes that additional intensification features of advanced reactive distillation technologies may help expand the operating regions, thus overcoming some of the limitations of reactive distillation. The technologies studied in this PhD thesis are briefly introduced in the next paragraphs.

A reactive dividing wall column (R-DWC) combines a reactive distillation (RD) column with a conventional distillation column using a dividing wall, taking further advantage of the functional domain. Compared to a conventional distillation sequence, a dividing wall column (DWC) presents advantages in terms of energy consumption, the number of vessels, and the capital cost required to achieve a specific separation (Mueller and Kenig, 2007). The R-DWC uses these advantages and extends the application for reactive systems with more than two product streams or where excess reactants need to be recirculated.

Catalytic cyclic distillation (CCD) incorporates a dynamic state in the operation of reactive distillation by manipulating the duration of an event (e.g., residence time), taking advantage of the temporal domain. In this case, rather than aiming for steady-state operation, a two-

step cycle is formed by a vapour-flow period – when the reaction takes place – and a liquid-flow period – when liquid flows from one stage to the next without remixing, facilitated by special internals enabling cyclic operation. The duration of the periods can be manipulated to allow favourable residence times to improve conversion (Bîldea et al., 2016).

Reactive high gravity distillation (R-HiGee) incorporates centrifugal fields created in rotating equipment – one of the approaches in the thermodynamic domain – to reactive distillation. As thin liquid films or tiny droplets are produced, the interface between the vapour, liquid, and solid phases is rapidly regenerated. Thus, mass and momentum transfer between the phases is enhanced, which favours phase separation (Cortes Garcia et al., 2017; Zhao et al., 2010).

Reactive internally heat-integrated distillation columns (R-HiDiC) combine the advantages of reactive distillation and internal heat integration and vapour recompression in distillation. Because heat transfer occurs simultaneously with reaction and separation, this is another example of the functional domain. Mechanical work is added to the system through a compressor to allow heat transfer from a colder heat source to a warmer heat sink. In other words, energy is transferred from the rectifying section to the stripping section, reducing demand for external utilities (Kiss and Ferreira, 2016).

Membrane-assisted reactive distillation (MA-RD) incorporates a membrane module to assist separation by overcoming azeotropes in the product streams of a reactive distillation column. Typical membrane separation mechanisms applied are vapour permeation and pervaporation, where the driving force for membrane separation is based on a difference in partial pressures or concentrations (Wankat, 2012). MA-RD is a further example of a functional domain (Lutze and Gorak, 2013).

1.1.2 Synthesis and design approaches for advanced reactive distillation

Process intensification needs to be incorporated into the synthesis and design of processes to develop more efficient and sustainable chemical process options (Skiborowski, 2018). Process synthesis aids the development of initial process flowsheets; process design defines operating conditions and sizes the main pieces of equipment. Several approaches have been proposed to introduce process intensification in the synthesis and design of processes to obtain feasible and beneficial configurations (Demirel et al., 2017; Holtbruegge et al., 2014a; Lutze et al., 2013). These approaches use heuristics, mathematical programming or a combination of both, known as a hybrid approach.

Process synthesis and design methodologies that consider hybrid units, such as reaction-separation systems, have been proposed in the research literature. However, solutions obtained from these methodologies typically include reactive distillation, rotating packed-bed reactors, and reactive absorption (Holtbruegge et al., 2014a; Niu and Rangaiah, 2016) as potential processing options, but advanced reactive distillation technologies are not featured. Garg et al. (2020) include non-conventional sources of energy such as microwaves and ultrasound, which is a means of addressing intensification. However, advanced reactive distillation technologies are not included in the case studies presented by Garg et al. (2020). Attempts to incorporate intensified units in retrofit have also been explored (Niu and Rangaiah, 2016; Perez-Cisneros et al., 2022).

Various methodologies combine the synthesis and design stages in a single procedure where the initial flowsheets are screened via mathematical programming (Skiborowski and Sudhoff, 2022), often requiring input models through coding and numerical solvers that can make the task computationally expensive (Alcántara Avila et al., 2021). The most common routes for mathematical programming are evolutionary modification methods or superstructure optimisation. In both cases, intensified technologies should initially be part of a large but finite set of technologies, also known as a knowledge base, database or portfolio (Lutze et al., 2012; Tian et al., 2018) or a superstructure that contains the optimal solution from the beginning (Barnicki and Sirola, 2004; Tylko et al., 2006). However, given the novelty and relative immaturity (i.e., low technology readiness level) of advanced reactive distillation technologies, these are often left out of the potential solutions.

In summary, existing approaches for developing new processes often cover a wide range of technologies, typically relying on conventional unit operations or well-established intensified units, such as reactive distillation (Kuhlmann and Skiborowski, 2017). In addition, conceptual design studies for advanced reactive distillation technologies often follow a technology-oriented procedure that limits their application to a case-specific basis. However, opportunities for capital and resource-efficient solutions are likely to be missed, as innovative technologies, such as advanced reactive distillation technologies, are often not considered. Therefore, it is necessary to develop new synthesis methodologies to realise the potential of advanced reactive distillation technologies more generally than current approaches, particularly during the development of the process flowsheet, applying a sound theoretical basis that supports later stages of detailed design.

1.2 Motivation

Incentives for applying conventional and advanced reactive distillation reported in the research literature are summarised in Table 1.1, which includes reference values for energy and capital savings, reduction in total annualised cost and reduction in plant size compared to conventional processes. The additional intensification of advanced reactive distillation technologies results in a reduction in the number of units, which may reduce capital expenditure. Also, energy consumption may be reduced due to internal heat integration and re-utilisation of energy generated within the system.

Table 1.1. Typical benefits of reactive distillation and advanced reactive distillation, compared to conventional reaction-separation-recycle flowsheets

Technology	Energy savings (%) ^a	Capital savings (%) ^a	TAC reduction (%) ^b	Size reduction ^c
RD	15–80	40–60	20–80	–
R-DWC	15–75	>20	>20	–
CCD	20–35	–	–	–
R-HiDiC	50–90	–	–	–
R-HiGee	No savings, but higher energy use	–	–	6–8 times
MA-RD	–	–	>30	–

^a Kiss et al. (2019), ^b Holtbrügge (2016), ^c Cortes Garcia et al. (2017)

Nevertheless, industrial implementation of advanced reactive distillation technologies is still scarce. This tendency could be attributed to the limited number of experimental demonstrations and the lack of a generally accepted methodology to integrate intensified technologies with the design of operable, safe and controllable configurations (Tian et al., 2020). Although a range of heuristics-based, optimisation-based and hybrid approaches for synthesis and design covering a large number of conventional and intensified technologies have been developed, advanced reactive distillation technologies are not yet accounted for. Due to the relative immaturity of these technologies, modelling and simulation resources are still scarce and yet to be developed. It is possible, however, to assess the benefits of additional intensification embedded in advanced reactive distillation technologies using relatively accessible information about the chemical system, heuristics, and first principles. This assessment will allow design engineers to quickly establish the technical feasibility of advanced reactive distillation technologies, so they can proceed to detailed design on a sound basis. Therefore, systematic methodologies to identify suitable intensified technologies are

necessary to rapidly screen the design space and develop process flowsheets in the early stages of process design (Orjuela and Orjuela, 2022).

This PhD thesis addresses the lack of synthesis methodologies that account for advanced reactive distillation technologies. The proposed methodology seeks to enable a quick, early-stage assessment of the technical feasibility of five advanced reactive distillation technologies (using first principles and heuristics based on thermodynamic properties and kinetic parameters of the chemical systems) to facilitate identifying trade-offs for technology selection with less computational effort than mathematical programming-based approaches. In this manner, the applicability of reactive distillation could be expanded in terms of operating conditions or the type of chemical systems to which it can be applied, resulting in a more resource-, capital- and energy-efficient operation and potentially avoiding the risk of missing promising solutions. This synthesis methodology could speed up the development of process flowsheets, including intensified technologies, and enable better-informed decisions regarding detailed process design.

1.3 Aim and objectives

This research aims to develop a systematic methodology to expand the applicability of reactive distillation by simultaneously assessing the technical feasibility of five advanced reactive distillation technologies and providing insights on their advantages and disadvantages that facilitate visualising trade-offs for technology selection during the process synthesis phase, while minimising requirements for process data and computational effort. The objectives set to achieve this aim are:

1. To examine the limitations of technology-oriented process design by identifying strategies used for the conceptual design of advanced reactive distillation technologies based on published studies
2. To identify data, interdependent phenomena and constraints that could be expanded upon to create a generalised approach applicable to the synthesis of advanced reactive distillation technologies by developing a conceptual design of a dual R-DWC
3. To define the scope, limitations and data relevant to the synthesis of advanced reactive distillation technologies in a conceptual framework by identifying basic thermodynamic properties and kinetic parameters and by formulating high-level questions using the conceptual design of a dual R-DWC and case studies reported in the literature

4. To identify and represent potential interactions between advanced reactive distillation technologies and chemical systems by extending the concept of operating windows to find and expand suitable operating regions and to test the proposed procedure with relevant case studies
5. To establish a synthesis methodology based on first principles and heuristics to qualitatively evaluate the advantages and disadvantages of advanced reactive distillation technologies applied to a chemical system to provide insights for the development of basic process flowsheets and to verify the validity of the results with industrially relevant case studies.

1.4 Structure of the PhD thesis

This PhD thesis is structured following the “Journal Format” according to the thesis policy of the University of Manchester. The thesis, therefore, incorporates scientific publications derived from this research and their corresponding Supplementary Information, as listed in Table 1.2. These publications are co-authored by the author of this PhD thesis and the supervisory team, Prof. Megan Jobson and Prof. Anton A. Kiss. Planning and execution, data acquisition, analysis and writing of the original drafts were performed by the author, while the supervisory team was involved in planning and supervising the research and reviewing the manuscripts.

Table 1.2. Details of publications presented in Chapters 3, 4 and 5

Chapter	Publication number	Publication details
3	1	Pazmiño-Mayorga, I., Jobson, M., Kiss, A.A., 2021. Conceptual design of a dual reactive dividing wall column for downstream processing of lactic acid. <i>Chem. Eng. Process. - Process Intensif.</i> 164, 108402. https://doi.org/10.1016/j.cep.2021.108402
4	2	Pazmiño-Mayorga, I., Kiss, A.A., Jobson, M., 2022. Synthesis of advanced reactive distillation technologies: Early-stage assessment based on thermodynamic properties and kinetics, in: Yamashita, Y., Kano, M. (Eds.), <i>Computer Aided Chemical Engineering, 14 International Symposium on Process Systems Engineering</i> . Elsevier, pp. 643–648. https://doi.org/10.1016/B978-0-323-85159-6.50107-X
4	3	Pazmiño-Mayorga, I., Jobson, M., Kiss, A.A., 2023. Operating windows for early evaluation of the applicability of advanced reactive distillation technologies. <i>Chem. Eng. Res. Des.</i> 189, 485–499. https://doi.org/10.1016/j.cherd.2022.11.048
5	4	Pazmiño-Mayorga, I., Jobson, M., Kiss, A.A., 2023. A Systematic Methodology for the Synthesis of Advanced Reactive Distillation Technologies. <i>Ind. Eng. Chem. Res.</i> 62, 5907–5928. https://doi.org/10.1021/acs.iecr.2c04540

The relationship between the research objectives presented in Section 1.3 and the chapters is explained in Figure 1.4. Note that there is some overlap and repetition between chapters, particularly when introducing the technologies and the proposed methodology, as each is a standalone publication.

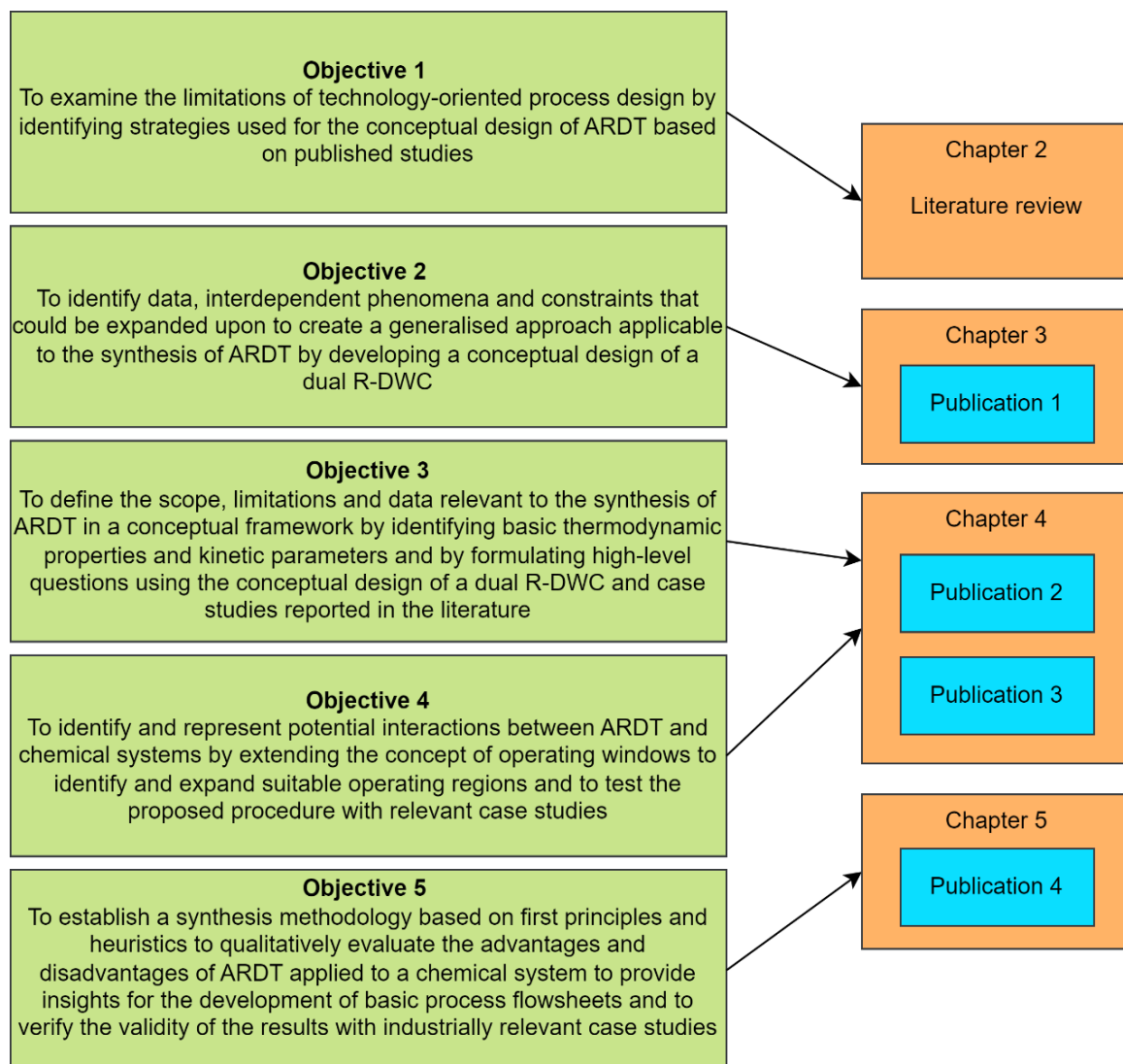


Figure 1.4. Relationship between the research objectives and Chapters 3, 4, 5

This thesis comprises six chapters. After the introduction in Chapter 1, Chapter 2 critically reviews the literature concerning process intensification, focusing on conventional and advanced reactive distillation. Process synthesis and design approaches for reactive distillation and advanced reactive distillation technologies are thoroughly reviewed. Then, a review of each of the advanced reactive distillation technologies is presented, focusing on their configuration, industrial applications and experimental investigations, and studies for their synthesis and design, closing with a general summary of the identified challenges and opportunities. Gaps in knowledge for the development of synthesis and design methodologies

accounting for advanced reactive distillation technologies are addressed in the research reported in this thesis.

Chapter 3 presents the first output of this research, Publication 1, a conceptual design study for a dual reactive dividing wall column – an example of an advanced reactive distillation technology – applied to purify lactic acid. The purpose of this study is to 1) explore the complexities of combined reaction and separation, 2) design and simulate an advanced reactive distillation technology, 3) identify the minimum required information to carry out the design and 4) elucidate the need for a systematic methodology to carry out the initial feasibility assessment of a particular technology. This conceptual design study of an intensified technology revealed some key issues that need to be addressed to develop a systematic methodology. Furthermore, this chapter contains Supplementary Information and a ‘Perspective on Publication 1’ section, which summarises the findings and learnings from the conceptual design study that are applied in the later chapters of the thesis.

Chapter 4 presents a conceptual framework (in Publication 2) that underpins the synthesis methodology using thermodynamic properties and kinetic parameters and proposing high-level questions. The ‘Appendix to Publication 2: Research approach for developing a synthesis methodology’ – which has not been published – discusses the use of case studies to underpin the research approach, the development of the methodology and the testing and verification of the resulting flowsheets. Publication 3 and its Supplementary Information present a procedure to build operating windows tailored for advanced reactive distillation technologies to identify appropriate ranges of operating conditions.

Chapter 5 presents the final output of this research, a systematic methodology for the synthesis of advanced reactive distillation technologies, in Publication 4, based on the conceptual framework and the evaluation of operating windows. The development and application of the methodology are then demonstrated in five industrially-relevant case studies. The results provide a ranking of advanced reactive distillation technologies, categorising them as advantageous, technically feasible and not applicable. In addition, the methodology suggests additional conventional unit operations to complement the operation. Then, novel process flowsheets that satisfy the design problem can be developed.

Finally, Chapter 6 presents the conclusions of this PhD thesis, including a critical analysis of the key findings and their implications, and makes recommendations for future research.

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Chapter 2

Literature review

The chapter begins with an overview of process intensification and its connection with process synthesis and design, focusing on reactive distillation. The next section examines the evolution of process synthesis and design approaches, focusing on reaction-separation operations that could lead to their application to advanced reactive distillation technologies. This is followed by a review of five advanced reactive distillation technologies in the scope of this PhD thesis, focusing on their configuration, advantages and disadvantages, investigations and applications, and modelling and design approaches used. After reviewing the literature, this chapter discusses the identified challenges and gaps and then outlines the research questions derived from the findings.

2.1 Process Intensification

To understand the role and potential of advanced reactive distillation technologies, it is useful to explore the benefits and advances of process intensification more generally.

2.1.1 Process intensification: An overview

Different interpretations and definitions of process intensification exist in the literature, often including terms that refer to a significant reduction in size, integration of functions, tasks or phenomena, or a function-oriented approach to process design (Stankiewicz et al., 2019). The term 'process intensification' first appeared in chemical processing in the mid-1960s to early 1970s, as stated by Stankiewicz et al. (2019). Early innovations regarding the use of rotation to enhance mass and heat transfer while significantly reducing the size of equipment appeared earlier in the 1920s (Reay et al., 2008). This focus on size reduction or 'miniaturisation' is emphasised in the definitions provided by Ramshaw (1983) and Dautzenberg and Mukherjee (2001).

This thesis focuses on the idea of the integration of functions (i.e., reaction and separation). To develop this idea, further intensification of reactive distillation and the advantages it can bring to the design of chemical processes is emphasised. For example, Tsouris and Porcelli (2003) and Stankiewicz and Moulijn (2000) discuss the concept of combining multiple

operations into fewer devices. From a performance point of view, Harmsen and Verkerk (2020) emphasise the advantages that integrated operations can provide over designs based on conventional unit operations.

The application of process intensification to the design of chemical processes can bring significant benefits. The most reported advantages of process intensification refer to increased energy efficiency and reduction in size and waste generation (Moulijn and Stankiewicz, 2017; Tian et al., 2018). Furthermore, less recycling leads to increased mass efficiency and decreased costs due to less piping and the reduced number of units (Harmsen and Verkerk, 2020; Stankiewicz et al., 2019). These advantages can contribute to improved economic and environmental performance. Reduced inventory and fewer transfer operations also improve safety, often reported qualitatively (Etchells, 2005; Ponce-Ortega et al., 2012). As reported by Etchells (2005), defining safety as an advantage is arguable since more integrated operations lead to challenges for operation and control. The disadvantages of intensification in an inherently safer process design are related to the dynamic controllability of the process resulting from small holdups and the inability to respond to disturbances in feed rates, utilities or external environmental factors, as explained in Luyben and Hendershot (2004). Other less-reported advantages include improvement in product quality, flexibility and simplicity, as summarised in Stankiewicz et al. (2019). As both intensified technologies and measurement methods are yet to be fully developed, these claims are debatable. As such, flexibility and simplicity could be improved by developing robust methods for designing intensified processes and assessing their performance.

A growing research interest in process intensification has been observed in academia with dedicated books and academic journals (Sitter et al., 2019), government-supported initiatives such as the European Roadmap for Process Intensification (2008) and the RAPID Institute in the United States (Bielenberg and Palou-Rivera, 2019) and industry, both with pioneering technology licensing companies and in-house developments, as highlighted in Harmsen and Verkerk (2020). Although there are commercial success stories (i.e., the methyl acetate process by Eastman), there is still a modest spread of intensified technologies and trained experts (Fernandez Rivas et al., 2020a). This trend has impacted education as process intensification is not typically part of the core modules in undergraduate degrees but is offered at the graduate level (Fernandez Rivas et al., 2020b).

2.1.2 Process intensification for process development

Process intensification is closely linked to process synthesis and design stages (Skiborowski, 2018). Process synthesis aims to develop initial process flowsheets, while process design provides operating parameters and equipment sizing (Seider, 2017). Therefore, implementing intensified technologies during process synthesis and design depends on the availability of suitable methodologies, models and tools that contribute to process development (Tula et al., 2020).

Different frameworks to incorporate process intensification in the design of chemical processes have been developed (Lutze et al., 2010; Van Gerven and Stankiewicz, 2009). In this PhD thesis, the study of advanced reactive distillation is analysed following the four domains proposed by Van Gerven and Stankiewicz (2009): functional, spatial, temporal and thermodynamic, briefly explained below (Stankiewicz et al., 2019):

- Functional domain: exploits interactions that occur when combining two or more functions (i.e., reaction and separation) in a single processing step. The combination aims to achieve a synergistic effect, which means that the impact of the combination shows better performance than each of the functions alone.
- Spatial domain: seeks to eliminate randomness at different scales (i.e., Brownian motion, pore distribution, random vs structured packing) by introducing spatial structures targeting molecular events, heat and mass transfer, and mixing and fluid flow.
- Temporal domain: introduces a transient or dynamic state in the operation by manipulating the duration of an event (i.e., characteristic times such as residence time, momentum or mass diffusion time, heat conduction time, and mixing time), creating a periodic or cyclic operation.
- Thermodynamic domain: uses alternative forms of energy (i.e., electric fields, high-gravity fields) to enhance heat and mass transport by changing how molecules are activated or separated.

The additional intensification features of advanced reactive distillation technologies are studied using the four domains proposed by Van Gerven and Stankiewicz (2009) to find opportunities to expand the applicability of reactive distillation. The term 'expand the applicability' refers to overcoming some of the limitations of reactive distillation, thus enabling broader application in terms of operating conditions or the type of chemical systems that can be applied. The insights from evaluating how each domain helps overcome the limitations of

reactive distillation, discussed in the following sections, are used to develop a systematic synthesis methodology that contributes to process development.

2.1.3 Process intensification in reactive distillation

Reactive distillation exploits the synergy gained by combining reaction and separation in a single column (Stankiewicz et al., 2019). Industrial examples of reactive distillation and the increasing number of scientific articles and patents on reactive distillation demonstrate the growing interest in developing this technology (Luyben and Yu, 2008; Orjuela et al., 2016). One of the most known examples of an industrial application of reactive distillation is the Eastman process for methyl acetate production, which is often reported in the literature (Luyben and Yu, 2008; Sundmacher and Kienle, 2003). The operation demonstrated an 80% reduction in energy consumption, and the construction required 20% of the initial investment of the conventional process as the number of units required decreased significantly (Siirola, 1996a). Other industrial applications of reactive distillation are reported (Kiss, 2016) but with little or no detail on their performance, unlike the Eastman methyl acetate process that has been used to demonstrate the potential of reactive distillation. Therefore, there is no definitive information about the take-up of the technology.

The advantages of reactive distillation come from the simultaneous reaction and separation. This combination allows azeotropes to be overcome, facilitating separation while improving reaction rates and selectivity, overcoming chemical equilibrium (Kiss, 2017). These advantages are translated into specific benefits such as (Ottewell, 2014; Sundmacher and Kienle, 2003):

- Conversion and selectivity are improved as a result of constant product removal
- Smaller plant footprint, since fewer units are required, providing capital cost savings
- Reduced energy consumption due to the use of exothermic heat of reaction for vaporisation of liquid
- Reduced recycle streams due to the integration of reaction and separation
- Improved safety due to reduced inventories and better control of runaway or side reactions
- Improved environmental performance due to reduced emissions associated with energy consumption
- Potential for overcoming difficult separations by incorporating a reactive entrainer (reactive separating agent) to promote a forward and reverse reaction

However, the range of operating pressures and temperatures needed for simultaneous reaction and separation, which must overlap, restrict the application of reactive distillation (Luyben, 2013; Seader, 2011). Moreover, the catalyst's thermal stability and life span further restrict the operating ranges (Orjuela et al., 2016). These boundaries are represented in operating windows (Kiss et al., 2019). An operating window is a graphical representation that allows for identifying feasible operation regions. Pressure and temperature as the two axes allow for representing equilibrium data associated with separations, reaction kinetics and the mechanical design of equipment (Recker et al., 2015; Schembecker and Tlatlik, 2003).

Operating windows are established in the field of chemical process design to identify potential economic trade-offs, reduce the design space and aid the initial evaluation of a potential processing option (Recker et al., 2015; Tylko et al., 2006). Details about the applications and features of operating windows are analysed in the introductory section of Publication 3 in Chapter 4. Other limitations of reactive distillation include the following:

- Unfavourable volatility preventing high concentrations of reactants and low concentrations of products in the reactive zone for economical operation (Keller, 2014; Luyben and Yu, 2008; Orjuela et al., 2016)
- Reduced number of degrees of freedom due to the combination of functions leading to decreasing operational flexibility (Stankiewicz et al., 2019; Tylko et al., 2006)
- Occurrence of reactive azeotropes where the net composition of the liquid and vapour phases do not change, which creates distillation boundaries making separation infeasible (Keller, 2014; Orjuela et al., 2016; Wierschem and Górak, 2018)
- Strongly non-linear process behaviour because of complex interactions between liquid, vapour and solid phases that make it difficult to represent mathematically relative volatilities, reaction driving force, heats of reaction, mass and heat transfer resistances, thermal sensitivity of the main and side reactions and catalyst stability (Keller, 2014; Orjuela et al., 2016)
- Multiple steady states because of the strong non-linear behaviour that results in different process outcomes under the same operating conditions that can impact operating costs (Keller, 2014; Wierschem and Górak, 2018)
- Large holdup volumes and trays are required for relatively slow reaction rates, which results in higher capital costs than those of a conventional configuration (Luyben and Yu, 2008)

- Highly endothermic or exothermic reactions can cause excessive condensation or vaporisation in the reactive zone that can impact vapour and liquid rates from stage to stage (Luyben and Yu, 2008)
- Time-consuming and expensive validations are required for industrial implementation because the column behaviour is scale-dependent due to variations in hydrodynamics, mass and heat transfer caused by the reactive packing (Orjuela et al., 2016)

Reactive distillation has limitations, but greater intensification (i.e., high-gravity fields, periodic operation, a further combination of functions) and appropriate selection of operating conditions, can help expand its applicability. In some cases, these changes can overcome the limitations of conventional reactive distillation, potentially extending its application to non-traditional chemical systems (Commenge and Falk, 2014; Kiss et al., 2019). This PhD thesis discusses the application of reactive distillation incorporating additional intensification techniques: advanced reactive distillation technologies (ARDT).

When modelling reactive distillation, the phenomena involved (i.e., mass transfer, fluid flow, phase equilibrium and reaction kinetics) can be represented mathematically using equilibrium-based or rate-based models (Noeres et al., 2003). In equilibrium-based models, it is assumed that chemical equilibrium is achieved; therefore, the chemical equilibrium constant is used to describe the chemical reaction (Taylor and Krishna, 2000). Mass transfer is not considered (Wierschem and Górak, 2018).

Rate-based models account for reaction kinetics and mass transfer rates, which are needed for detailed designs where descriptions of multicomponent mass transfer, reaction kinetics, hydrodynamics, non-ideal thermodynamic behaviour and heat transfer are considered (Sundmacher and Kienle, 2003; Taylor and Krishna, 2000). Once rigorous models are defined, these are used to calculate the mass and energy balances to calculate process performance. These models can be implemented in computer-aided tools to automate calculations (Seider, 2017; Tian et al., 2018).

2.1.4 Barriers to the implementation of intensified technologies

Past and ongoing research in process intensification has demonstrated the benefits it can bring to the development of efficient chemical processes, as discussed in section 0. However, questions and challenges remain about the implementation and uptake of intensified technologies. The barriers to the implementation of intensified technologies are analysed from methodological and practical points of view.

From a methodological point of view, modelling and simulation are inherently challenging due to the complexity of the systems (Kiss et al., 2019). Automated calculations are enabled through computer-aided tools that include equation solvers (input the models through coding) and model-based rigorous process simulators (embedded equation solvers, models and databases) (Martín, 2016; Seider, 2017). Aspen Plus, a commercial process simulator, offers a rigorous model to simulate different vapour-liquid unit operations, including reactive distillation: RadFrac (Aspen Technology, Inc, 1999; Skiborowski, 2018). The RadFrac model can handle different types of reactions (kinetic, equilibrium and electrolytic) in the liquid or the vapour phase (Venkataraman et al., 1990). However, models to represent advanced reactive distillation technologies are lacking. The unavailability of simulation tools for these “niche” applications could be attributed to the absence of industrial applications, lack of model validation (Skiborowski, 2018), and low demand from users to implement intensified units (Bielenberg and Bryner, 2018). Modelling and simulation investigations for the design of advanced reactive distillation are detailed for each technology in section 2.3.

From a practical point of view, a general lack of familiarity with intensified technologies at the enterprise and management levels may be linked to risks associated with commercialising breakthrough technologies that are not as predictable as conventional units (Boffito and Fernandez Rivas, 2020). In order to fully penetrate chemical process industries, solutions from process intensification need to expand in scope, scale, and methodologies, possibly offering solutions tailored to retrofitting existing equipment (Patel and Pereira, 2022). In addition, the long development path, concerns about safety, and the need for regulatory requirements to stimulate process innovation of novel technologies also limit the spread of intensified technologies (European roadmap of process intensification, 2008; Sitter et al., 2019). Operability and controllability of intensified technologies present challenges due to the loss of degrees of freedom as a result of the integration of functionalities, narrower operating windows and faster process dynamics (Pistikopoulos et al., 2021a). The lack of historical data (e.g., cost estimation, safety evaluation), heuristics and guidelines associated with process operations present a challenge for the practical operational performance that can lead to control infeasibilities (Gazzaneo et al., 2019). In the case of reactive distillation, an alternative to overcome controllability issues is to perform design and control simultaneously to identify and eliminate promising design alternatives that may have controllability problems (Iftakher et al., 2021). Nevertheless, there is a need to develop a formal theory and fundamental understanding of operability and controllability in process intensification. In addition,

developing operability and control metrics at an early design stage that account for tight integration could be beneficial to ensure operational performance and accelerate technology development (Pistikopoulos et al., 2021a).

The following section presents an overall introduction to process synthesis and design approaches for reactive distillation and hybrid reaction-separation units.

2.2 Process synthesis and design of advanced reactive distillation

Process synthesis and process design are two closely related tasks supporting process development. Similarly, the field of Process Systems Engineering (PSE) combines mathematical modelling, optimisation and control to improve decision-making to aid in the design, manufacture, and distribution of chemical products by integrating systematic procedures for designing and operating chemical processes at multiple scales (e.g., microsystems and industrial systems) (Grossmann and Westerberg, 2000; Pistikopoulos et al., 2021b). As a means to extend the scope of PSE, process intensification is seen as a mechanism to integrate process synthesis and design to obtain reliable and innovative alternatives (Skiborowski, 2018). Despite the increasing trend in process intensification research, these studies are still behind the core PSE tools – process synthesis, optimisation, and control – as well as combined studies that address these tools simultaneously with process intensification, as noted by Alcántara Avila et al. (2021).

The synthesis and design of reactive distillation – chemical processes in general – use heuristics-based, optimisation-based methods or a combination, known as hybrid methods.

- *Heuristics-based methods:* Also known as rule-based methods, use empirical generalisations derived from observations that provide insights to start a design or to verify the validity of a result. Heuristic rules, typically applied in the synthesis stage, are handy tools to initialise a design without extensive calculations and for troubleshooting in chemical engineering (Turton, 2018). Still, they are sometimes difficult to justify and do not always guarantee a solution.
- *Optimisation-based methods:* Use mathematical programming to improve the performance of a process by minimizing or maximizing an objective function varying the available degrees of freedom using a systematic procedure (Ponce-Ortega and Hernández-Pérez, 2018; Westerberg, 2004). Optimisation techniques applied to an initial process flowsheet include structural and parameter optimisation. Another technique is a reducible superstructure with redundant features where the unnecessary

elements are eliminated (Smith, 2016). A limitation of superstructure-based approaches is that the initial superstructure needs to capture all the desired alternatives or contain the optimum in the first place. Also, solving large optimisation problems can be computationally expensive (Alcántara Avila et al., 2021; Barnicki and Sirola, 2004).

Starting from a solution based on existing processes, evolutionary modification through mathematical optimisation performs targeted modifications, typically applied for retrofit. However, this approach depends on a finite but large set of alternatives (also termed knowledge base, database, or portfolio) which should contain the intensified technologies. Search methods typically applied to reactive distillation design are non-linear programming (NLP) and mixed-integer non-linear programming (MINLP) because reactive distillation models are highly non-linear due to the complexity of the system and the introduction of integer variables to allow discrete decisions (e.g., the number of trays), often including economics (Tian et al., 2018).

- *Hybrid methods:* Integrate heuristics and mathematical optimisation in various stages of process synthesis and design to overcome the limitations of each approach when applied individually. Traditional heuristic or rule-based approaches can be combined with improved process models, numerical solver algorithms, and mathematical programming (Pistikopoulos et al., 2021b). Heuristics are typically used for the process synthesis stage, and the results are used to initialise simulations or to help optimise a superstructure (Tylko et al., 2006).

Although both synthesis and design are part of the fundamental layer of PSE, Pistikopoulos et al. (2021b) argue that process synthesis applied to flowsheet development has had limited use in education and practice and only specific applications in research, whereas the development of process design for sizing and costing has been widely used. For example, an approach for strategic process synthesis proposed by Sirola (1996b) had an important impact on understanding hybrid units, as demonstrated in an application for methyl acetate production. However, this approach has not had a practical application for process synthesis.

In the literature, a term to refer to the combination of functions (e.g., reaction, separation) in a single device is not always clear. These units are interchangeably called hybrid, multifunctional, integrated or intensified. Babi et al. (2016) define the term ‘hybrid/intensified unit’ as “an operation that enhances the function of one or more unit operations performing a task or a set of tasks through a new design of the unit operation or the combination of more

than one unit operations". Throughout this PhD thesis, the term 'hybrid unit' is used to refer to units that combine different functions, particularly reaction and separation, while the term 'intensified unit' is used more generally to refer to units taking advantage of process intensification more broadly, beyond the combination of functions.

The next sections provide a brief introduction to process synthesis and process design, focusing on the introduction of process intensification, particularly for reactive distillation. Next, a critical review of the existing methodologies for synthesis and design of combined reaction-separation is provided. The progress made on the synthesis and design of advanced reactive distillation technologies is described individually for each technology in section 2.3.

2.2.1 Process synthesis: initial screening and flowsheet development

Process synthesis aims to assemble initial process flowsheets that transform raw materials into valuable products. This task, typically based on empirical rules gained from experience and insights at the unit operations scale that helps screen the design space (Sitter et al., 2019; Turton, 2018), is done by selecting the major pieces of equipment and their arrangement, including recycling streams, in a process flowsheet. (Seider, 2017; Turton, 2018). Rudd et al. (1973) proposed one of the earliest approaches to process synthesis as a way to analyse a process as a whole by considering the potential interactions between its elements. Another widely known approach is that of Douglas (1985), also known as the onion model of Linnhoff et al. (1982), who proposed a hierarchical approach that decomposes the overall synthesis problem as a hierarchy of subproblems. Here, the solution begins with reactor design, while the synthesis of separation and recycle systems, heat recovery systems, utility systems, and waste and effluent treatment are solved subsequently. Though the hierarchical approach has been widely used for process synthesis and design, the logic proposed does not work for intensified units, according to Skiborowski and Sudhoff (2022). This is due to the integration of functions or units that aim to use the synergy of the combined operation.

When using a manual approach to process synthesis, flowsheet generation and analysis are limited. However, applying a computer-aided software tool allows multiple flowsheet alternatives to be generated and screened efficiently and reliably, as noted by Tula et al. (2018). Hence, algorithm-based methods, often including mathematical optimisation, have been developed for process synthesis (Skiborowski and Sudhoff, 2022), particularly those that incorporate intensified technologies (Tian et al., 2020), which are discussed in section 2.2.4.

2.2.2 Process design applied to reactive distillation

While process synthesis focuses on the structural aspects of the process flowsheet, the design of reactive distillation systems involves the evaluation of the behaviour of different configurations by varying key variables (degrees of freedom) to achieve the objectives posed by the design problem. The degrees of freedom relevant to reactive distillation are discrete (e.g., the number of stages (reactive, stripping and rectifying) and the location of the feed(s)) or continuous variables (e.g., reflux ratio, reboiler duty, operating pressure and tray holdup) (Luyben, 2013; Sundmacher and Kienle, 2003). The tray holdup plays an important role in reactive distillation as it affects conversion, product composition and composition profiles (Luyben, 2013). Finally, the design specifications for reactive distillation are the product(s) composition and the reactant conversion (Kiss, 2013).

When designing advanced reactive distillation systems, the number of degrees of freedom reduces because of the complex interconnections in intensified units, as opposed to conventional unit operations (Baldea, 2015). Methodologies for the design of reactive distillation systems have limited applicability for advanced reactive distillation technologies due to simplifying assumptions and the fact that their additional intensification features are not considered. For example, design guidelines for reactive distillation proposed by Subawalla and Fair (1999) assume constant molar liquid holdup at each stage and do not take into account the characteristics of the catalytic column internals.

Designing reactive distillation processes can be performed via graphical, heuristic and optimisation approaches, each featuring key assumptions, advantages, and disadvantages.

2.2.2.1 Graphical methods

The reactive residue curve map allows an understanding of reactive distillation when a reaction occurs in the liquid phase (Barbosa and Doherty, 1988; Beneke, 2013; Ceaşescu et al., 2015). Muthia et al. (2018) proposed an applicability graph suited for quaternary systems exhibiting a near-ideal behaviour to assess the feasibility of reactive distillation without rigorous simulations. Unlike residue curve maps that have been applied in industry to analyse azeotropic systems in distillation (Siirola, 1996a), reactive residue curve maps application has been evidenced in research studies only (Velandia et al., 2021; Zheng et al., 2018) as limited information about reactive distillation is disclosed on the open literature. Also, boiling point rankings have been proposed to identify opportunities to separate certain species by distillation simultaneously with reaction (Luyben and Yu, 2008).

2.2.2.2 Heuristic approaches

Kiss et al. (2011) offered a systematic approach to evaluate the technical and economic feasibility of reactive distillation, including the recommendation of R-DWC as a viable alternative during a feasibility analysis in one of the case studies. Shah et al. (2012) proposed a systematic framework to evaluate the economic and technical feasibility of reactive distillation, where the latter used the Damköhler number (Da), chemical equilibrium constant (K_E) and Hatta number (Ha).

2.2.2.3 Optimisation approaches

With the advent of increased computing power – powerful solvers, high-performance computing, and quantum computing – process design has also been proposed using superstructure optimisation (Douglas and Sirola, 2001). Lutze et al. (2013) proposed one of the first approaches to process synthesis incorporating process intensification following a phenomena-based approach, using building blocks rather than a conventional unit operation. Building blocks represent fundamental elements of unit operations, which can host single or multiple phenomena. Combining these phenomena aids in representing operations, processing units, flowsheets, and superstructures. Feasibility and performance checks are conducted on solutions considering additional operational constraints concerning the unit operation level. This approach is applied in various synthesis and design methodologies, which include intensified technologies such as reactive distillation, aiming to obtain optimal designs, detailed in section 2.2.4. High-performance computing can be used to quickly solve large-scale optimisation problems, although new computing algorithms and decomposition schemes are required (Daoutidis and Zhang, 2022). Another application of high-performance computing, with artificial intelligence, is to bring process-scale insights into research and development at the laboratory scale (i.e., catalytic reaction engineering, process optimisation, multiscale modelling) and use literature data and automation to guide process development (Batchu et al., 2022). Quantum computing offers capabilities to solve integrated product and process design problems such as property prediction, complex multi-step chemical reactions, solid catalyst design, solvent design and molecular dynamics (Andersson et al., 2022).

2.2.2.4 Hybrid approaches

While heuristic-based approaches are useful for initial screening during the synthesis stage to produce suitable processing options, other techniques, such as superstructure optimisation, are typically used as a finishing step to obtain an optimal design. The work of Almeida-Rivera

et al. (2004) identified the advantages and limitations of graphical, optimisation and heuristic approaches, which are then summarised in a qualitative fingerprint matrix to facilitate comparison between them. Finally, they combine graphical and optimisation approaches to overcome each other's limitations and propose a hybrid approach.

The use of heuristic methods as a standalone procedure or combined with mathematical programming applied for hybrid units, particularly reaction-separation systems, is detailed in section 2.2.4.

2.2.3 Heuristics relevant to advanced reactive distillation

Heuristics remain a valuable tool, particularly in industrial practice, to provide guidance for potential processing options (Skiborowski and Sudhoff, 2022; Westerberg, 2004). This section describes heuristics reported in the literature used for reactive separations, vapour-liquid separations, and reactive distillation systems, which can provide valuable insights for the synthesis and design of advanced reactive distillation technologies.

For reactive separations, especially useful for reversible reactions:

- Remove the reaction products so the reactions are driven to completion to promote different distributions of chemicals (Seider, 2017).

To separate vapour-liquid mixtures, recommendations applied to distillation include:

- Avoid extreme temperatures, for example, a low-temperature separation that requires refrigeration or a high-temperature separation that could be detrimental to heat-sensitive materials (Seider, 2017).
- Avoid extreme pressures that require gas compression or vacuum because the capital investment increases (Seider, 2017).
- Pressure in conventional distillation design is usually set by a minimum temperature in the reflux drum (to use cooling water) or a maximum temperature in the reboiler (to prevent fouling or thermal decomposition). Establishing the optimum pressure in a reactive distillation column is more complex because of the interplay between reaction and phase separation (Luyben, 2013).

A hypothetical quaternary system (representative of an equilibrium-limited reaction) is used for reactive distillation. It assumes ideal vapour-liquid equilibrium (relative volatilities are kept constant), constant operating pressure, no pressure drop, exothermic reaction and equimolar feed. Heuristics obtained from the above scenario are:

- Place the reactive zone where the reactant concentration is high
- Prefer arrangements where the reactants are intermediate components
- Prefer systems where the relative volatility between the reactants is low and between the products is high.

These suggestions do not mean other arrangements are impossible. They would require higher capital investment due to larger reactive zones required, larger separation zones (stripping and rectifying), or higher reflux ratios or boilup ratios that result in high energy consumption (Luyben and Yu, 2008). Overall, these heuristics and simplifications used to represent complex systems have been applied in investigations to develop methodologies for reactive distillation, such as using boiling point rankings for the applicability graph proposed by Muthia et al. (2019).

Kiss (2013) provides a comprehensive review, including useful heuristics for design and control, of advanced distillation technologies, namely dividing wall columns, heat pump-assisted distillation, HiGee distillation, heat integrated distillation column, cyclic distillation and reactive distillation. While advanced reactive distillation technologies do not have specific heuristics, this PhD thesis interprets heuristics proposed by Kiss (2013) and those obtained from case-specific investigations to support the development of synthesis methodologies by extending their application to advanced reactive distillation technologies, discussed individually in section 2.3.

2.2.4 Methodologies for intensified technologies with a focus on hybrid reaction-separation

Methodologies reported in the literature introducing process intensification, particularly focused on hybrid reaction-separation, are discussed below. General approaches (e.g., heuristic, mathematical programming, hybrid), scope (e.g., synthesis, design, retrofit) and their limitations are also explained.

2.2.4.1 Synthesis of flowsheets

Process synthesis approaches focused on hybrid units, particularly reaction-separation systems, have also been explored by researchers. Focusing on the synthesis of a whole process, as opposed to a single integrated reaction-separation unit, Schembecker and Tlatlik (2003) introduced a general process synthesis procedure that evaluates the interaction of the integrated reaction-separation unit with the whole flowsheet. The process is deemed feasible if the reaction, separation, and apparatus windows overlap. Acknowledging the challenges of

screening a wide spectrum of processing alternatives, Tlatlik and Schembecker (2005) proposed a generic 'phase model' approach for multifunctional units to gain a general understanding of complex separation and reaction operations as proper simulation studies are often limited by the lack of rigorous models and the unavailability of complete sets of thermodynamic and chemical parameters. While the methodologies of Schembecker and Tlatlik (2003) and Tlatlik and Schembecker (2005) focused on developing feasible process flowsheets, Tylko (2006) combined heuristics to define an initial configuration. Then, a superstructure is optimised, assuming that the optimal solution is contained, so the large design space for reaction-separation processes is addressed.

2.2.4.2 Heuristics-based method for retrofit

Perez-Cisneros et al. (2022) proposed a three-step rule-based method for retrofitting conventional processes using intensified units, focusing on reactive distillation, reactive dividing wall column and hybrid distillation schemes. Three sets of questions, one for each technology, allow for an initial assessment of the technology for a feasibility check. Since the approach is tailored for retrofitting applications, substantial previous knowledge and expertise are required.

2.2.4.3 Hybrid methods for synthesis and design

Departing from a flowsheet based on previous configurations for the design of integrated reaction-separation processes, Recker et al. (2015) proposed a three-step methodology using 1) experts' knowledge and heuristics, 2) shortcut methods for operating costs estimation and 3) a rigorous deterministic approach using initialisation values from the previous steps. Although these methodologies focus on the synthesis and design of processes containing hybrid units, their use is not directly motivated, as process synthesis approaches still focus on conventional unit operations, as noted by Kuhlmann and Skiborowski (2017). This suggests that advanced reactive distillation technologies would only be considered if they are included in the initial superstructure or if they have been considered in previous flowsheets, resulting in isolated solutions that may not be applicable in other situations.

Using thermodynamic insights (identification of physical and chemical properties and potential for exploiting the available driving forces), Jaksland et al. (1995) proposed a synthesis method for generating physically suitable flowsheets for separation processes. The analysis is represented in a binary ratio matrix to simplify the separation problem by defining binary or multicomponent splits and identifying feasibility limits. This approach has been applied as a

basis for developing methodologies focusing on process intensification. For example, Holtbruegge et al. (2014a) extended the thermodynamic insights approach of Jaksland (1995) to incorporate hybrid and reactive separations. This approach generates flowsheet options and finds the best option through optimisation. During the first stage, conventional and intensified operations widely applied in the chemical industry, available in a so-called 'portfolio', are identified and analysed. Due to the low technology readiness level of advanced reactive distillation technologies, they are not featured in the portfolio. Similarly, Lutze et al. (2012) developed a computer-aided model that incorporates thermodynamic insights to identify the best options through mathematical programming based on a set of previously known intensified technologies.

While sustainability is typically evaluated at the last stage of process synthesis, Demirel et al. (2017) and (2020) proposed multi-objective optimisation to introduce intensified options and sustainability at the phenomena level using building blocks. This approach allowed the identification of reactive distillation and heat-integrated partially intensified reactive distillation. Using thermodynamic insights (Jaksland et al., 1995) to drive the identification of phenomena building blocks (Demirel et al., 2017; Lutze et al., 2013), Garg et al. (2020) describe a systematic methodology for the simultaneous synthesis and intensification of existing and new process flowsheets. A task-based superstructure is translated into unit operations to create a phenomena-based superstructure that is first reduced by applying feasibility and logical rules and combinatorial algorithms. Then, mathematical programming is used to determine the feasible combinations leading to flowsheets. The methodology proposed by Garg et al. (2020) covers a wide range of features that are usually dismissed, for example, solid phase and non-conventional sources of energy (microwaves, ultrasound). Also, the authors claim that this methodology is one of the first to create new flowsheets without using pre-existing processes.

2.2.4.4 Mathematical programming-based methods for synthesis, design and retrofit

To overcome the issue of requiring previous knowledge about intensified units, a phenomena-based synthesis and design methodology was proposed by Lutze et al. (2013), previously discussed in section 2.2.2. With a focus on sustainable process synthesis and intensification, Babi et al. (2015) used the phenomena-based synthesis approach of Lutze et al. (2013) to generate flowsheet alternatives that contain intensified operations at the unit operations scale using a 'knowledge base' of potential phenomena-building blocks. The results of a case

study demonstrated that intensified operations show better performance than conventional configurations in terms of economics, sustainability metrics and life cycle assessment factors. Following a similar approach, Anantasarn et al. (2017) reached similar conclusions. Other methodologies based on a portfolio of predefined phenomena building blocks have also been proposed (Kuhlmann et al., 2018; Kuhlmann and Skiborowski, 2017). However, simultaneous phenomena building blocks, which are set with predefined rules, do not evidence the introduction of other forms of intensification, such as high-gravity fields, opportunities for internal-heat integration or cyclic operation. At the same time, process design requires rigorous models, which are not yet fully developed for the technologies in the scope of this PhD thesis.

Superstructure optimisation can include aspects such as economics, sustainability, safety, and circular economy. For example, Castillo-Landero et al. (2019) start with a base case design. Then gradual integration is performed in each step to obtain an intensified design with a minimum number of units. Li et al. (2020) integrated power and water supply and water treatment in superstructure optimisation approach for synthesis and design. They start with a hierarchical approach to process synthesis, then superstructure creation with a finite number of processing units and interconnections, formulation of the optimisation problem as MILP or MINLP, and finally, solutions of the optimisation problem to obtain optimal topology and process parameters.

Focusing on retrofitting applications using intensified units, Niu and Rangaiah (2016) proposed an optimisation-based approach with and without intensified units, focusing on the suitability of reactive distillation and reactive absorption. A retrofit solution pool is mentioned, but it is mostly a combination of a reactor and a 'contributing unit' (e.g., a separation unit) or two separation units.

2.2.4.5 Critical review

As discussed so far, there appears to be a tendency to disregard the application of heuristic-based approaches and instead rely on PSE tools, such as mathematical optimisation. Costa and Bagajewicz (2019) assert that process designers do not need to develop expertise to implement a conceptual design (due to time limitations), so computer optimisation would be easier to use relying on the embedded models. Similarly, Meramo-Hurtado and González-Delgado (2021) consider that an engineer's opinion is biased or subjective, while they also claim that superstructure-based approaches that use building blocks are practical, particularly

for process intensification. These ideas suggest that process understanding to anticipate potential interactions of a particular system is not essential when developing a new process, especially when using generalised models or computer tools.

While heuristics may contradict each other and not help the decision-making process to find an optimal configuration, the objective is to find potentially feasible solutions and avoid trial-and-error methods focused on a case-specific basis. The use of heuristics can be of special interest when a particular phenomenon cannot be expressed mathematically to be included in the models. In addition, heuristics and experience from other processes can contribute to process development, which is the case for advanced reactive distillation technologies where the technology readiness level is generally low – the technology concept has been formulated at the least and up to pilot scale demonstrations at the most, with only a few cases implemented industrially (Kiss et al., 2019).

The following section discusses the main features of advanced reactive distillation technologies, emphasising those potentially expanding the applicability of conventional reactive distillation.

2.3 Advanced reactive distillation technologies

This section describes the advanced reactive distillation technologies covered in this PhD thesis, highlighting the domains of process intensification relevant to each technology, their configuration and operation, examples of industrial applications and experimental investigations, including heuristics identified, and methodologies applied for their synthesis and design. Finally, this section closes with an overview of the challenges identified.

2.3.1 Reactive dividing wall column

The reactive dividing wall column (R-DWC) combines already integrated technologies: dividing wall column (DWC) and reactive distillation (RD) (Weinfeld et al., 2018). The R-DWC consists of a single vessel with a wall that divides the column into the feed and product sides, illustrated in Figure 2.1. Each section contains internals that promotes contact between the vapour and liquid flowing upwards and downwards. The location of the feed streams, dividing wall, and reactive zone can lead to additional configurations (Mueller and Kenig, 2007; Weinfeld et al., 2018). Additionally, the use of homogeneous catalysts has also been reported (Weinfeld et al., 2018).

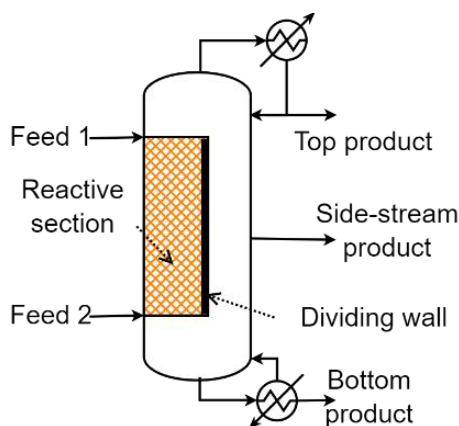


Figure 2.1. Main features of an R-DWC (adapted from Weinfeld et al. (2018))

The main advantages of a DWC over conventional distillation sequences, extended for an R-DWC, are a reduction in energy consumption due to the higher thermodynamic efficiency than that of multiple column arrangements, as the wall avoids lateral mixing of middle boiling components, as well as a reduction in the number of distillation columns required to achieve a particular separation, which results in capital costs savings (Asprion and Kaibel, 2010; Kiss, 2016). In chemical systems with multiple products or that require recycling of excess reactant, R-DWC offers a significant advantage in removing middle boiling products as side streams (Mueller and Kenig, 2007). This characteristic is key to managing multiple splits and outlet streams in a reaction-separation system. However, an R-DWC can operate at one given pressure, as opposed to the operation in separate columns where the operating pressure can be set independently, which reduces its degrees of freedom. Reducing the number of vessels also results in requiring fewer but larger condenser and reboiler, which operate at the most extreme temperatures of the chemical system. Finally, the control of internal flow, particularly the vapour split, is challenging in practice as the pressure drop across different sections around the wall can vary due to the location of catalytic packing and the placement of the dividing wall (Schröder et al., 2016; Weinfeld et al., 2018).

Unlike DWC industrial implementation, starting with the first documented industrial installation at a BASF site in 1985 (Kiss, 2016; Montz, 2019) and a range of retrofits, with Montz as one of the leading DWC technology providers (Hoyme, 2017), R-DWC has not been implemented at a similar pace. An industrial application of R-DWC is attributed to AkzoNobel, where an undisclosed system containing seven components, five chemical reactions and three binary azeotropes is treated to obtain a pure intermediate-boiling product. This configuration provides savings of 36% in capital costs and 15% in energy costs (Hoyme, 2017).

The application of R-DWC has been investigated in quaternary systems featuring equilibrium-limited reactions such as esterification (An et al., 2015; Delgado-Delgado et al., 2012; Hernández et al., 2009; Kiss et al., 2012; H. Li et al., 2019) and transesterification (Mueller and Kenig, 2007). The species evaluated range from short-chain organic acids such as acetic acid to long-chain fatty acids such as lauric acid. Etherification reactions with two reactants and one product have also been investigated (Kaur and Sangal, 2018; Kiss and Suszwalak, 2012).

A range of approaches for modelling R-DWC covers equilibrium stage models based on MESH equations and rate-based models that account for mass and heat transfer and hydrodynamics. The design methodologies for an R-DWC are extended from those to design conventional DWC. Sun and Bi (2014) extended the application of the minimum vapour flow method (based on the Underwood equations) and the minimum-energy mountain diagram to the R-DWC by considering the effect of the reaction. Daniel et al. (2006) used the boundary value method (compositions set at the ends of the column) for the conceptual design of an R-DWC.

Since no commercial simulator provides an R-DWC module, not even for a DWC, a decomposition method is typically used for simulation. The R-DWC is separated through the dividing wall in a sequence of conventional and reactive distillation columns with interconnecting streams to form a system thermally and hydraulically equivalent to an R-DWC (Schröder et al., 2016; Weinfeld et al., 2018). When constructing the R-DWC configuration, the mass-transfer resistances of all components are assumed to be identical, and heat transfer through the wall is assumed to be negligible (Novita et al., 2018). The decomposition of R-DWC results in a pre-fractionator containing the reactive section (feed side of the R-DWC) and a main column containing the reboiler and the condenser (product side of the R-DWC) (Weinfeld et al., 2018). The initialisation of rigorous simulations requires starting guesses for the design variables, which are obtained from simpler models containing a conventional RD column followed by a direct or indirect distillation sequence (Weinfeld et al., 2018). Egger and Fieg (2019) propose equations for an equilibrium model and a non-equilibrium model implemented in Aspen Custom Modeler V8.4 for a reactive dividing wall column. The equilibrium model provides higher accuracy predictions for product compositions and reactants conversion, which is suitable for the initial design. The non-equilibrium model offers more accurate information about the internal column behaviour, such as temperature and concentration profiles, which is adequate for detailed design. Experimental data at the pilot

scale successfully validated the proposed models, positioning R-DWC as an operable, controllable and efficient intensified unit.

Kiss et al. (2019) suggest that the experience and methodologies developed for designing DWC and RD constitute a solid basis for expanding their application to an R-DWC, which may lead to a process with energy savings, a smaller number of units and improved outputs. However, several challenges remain to be further developed regarding the modelling and simulation of R-DWC as there exist uncertainties about the decomposition methods, complex control schemes for the improvement of dynamic models and experimental demonstrations that allow proving this concept for industrial implementation (Dai et al., 2022; Weinfeld et al., 2018).

2.3.2 Reactive high-gravity distillation

Reactive high-gravity distillation (R-HiGee) combines two already intensified technologies: high-gravity distillation (HiGee) and rotating packed-bed reactors (RPB) (Cortes Garcia et al., 2017). Figure 2.2 illustrates the main parts of an R-HiGee unit: a casing contains rotating discs that support the packing, containing a solid catalyst. The liquid feed enters through the rotor and travels outwards, while the vapour feed enters in the casing side and travels inwards — the liquid and vapour travel counter-currently through the catalyst. The vapour and liquid products leave the unit from the upper centre and the bottom, respectively (Cortes Garcia et al., 2017; Kiss et al., 2019).

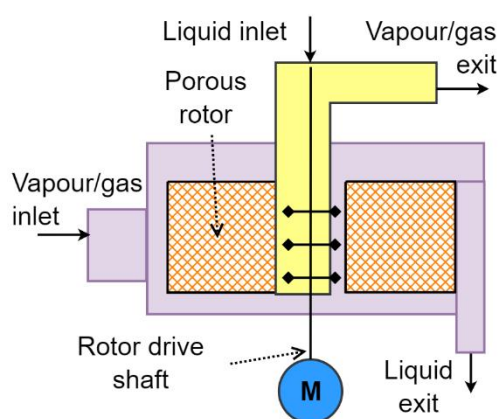


Figure 2.2. Schematic of an R-HiGee (modified from Quarderer et al. (2000))

R-HiGee technology offers advantages due to high centrifugal forces that enhance catalyst wetting to favour the reaction and improve mass transfer to favour phase separation (Kiss, 2016). As a result of the high rotational speed, residence time and holdup volume decrease. This reduces the size of the equipment, in turn enabling modularisation (Kiss et al., 2019). Due to the small liquid holdup and rapid mass transfer, undesired series reactions that reduce

selectivity towards the desired product can be avoided as rapid removal of the main reaction products is possible (Sudhoff, 2022a). This characteristic requires the main reaction to be relatively fast, so good conversion is achieved (Quarderer et al., 2000). Despite specific studies showing effective heat dissipation for HiGee distillation (Illner et al., 2022), Rao (2022) suggests that HiGee is unsuitable for reactive separations involving large heats of reaction because in situ cooling or heating are difficult. Alternatives to reduce hot spots in rotating packed beds include using coils for heating and cooling, which is reported for gas absorption (Neumann and Wenzel, 2022). Poor heat dissipation could be attributed to unfavourable geometries and the reduced contact time between the vapour and liquid phases. Hence, R-HiGee is limited to systems involving low heat effects (Rao, 2022). From an operational point of view, rotating parts and packing supporting the catalyst may be vulnerable to long-term reliability concerns due to mechanical considerations (e.g., bearing loads, vibration moments), which may require more frequent preventive and corrective maintenance (Cortes Garcia et al., 2017).

The operation and compactness of HiGee devices could allow their application in situations where there is movement or restricted space, for example, off-shore platforms and spacecraft (Cortes Garcia et al., 2017; Long et al., 2016; Reay et al., 2008). Niche applications for R-HiGee include high-viscosity fluids or reactions that are fast and mass transfer controlled (Gudena et al., 2012; Long et al., 2016; Rao, 2022). An industrial application of R-HiGee is when one of the reactants is a gas, similar to gas stripping, except the gas reacts in contact with the liquid phase and catalyst. This application led to the industrial production of hypochlorous acid at Dow Chemical (Cortes Garcia et al., 2017; Quarderer et al., 2000). It has been reported that reactive HiGee precipitation for the preparation of nanoparticles (Zhao et al., 2010) and HiGee distillation, stripping and gas cleaning have been applied industrially in China (Rao, 2022). However, limited information about industrial applications of R-HiGee is available in the open literature. R-HiGee has been investigated for the esterification of short-chain organic acids and long-chain alcohols (Gudena et al., 2012; Krishna et al., 2012).

The existing modelling attempts for R-HiGee include both equilibrium and non-equilibrium approaches. Detailed models account for changes in mass transfer coefficients along the radius due to the gravity field, interphase mass transfer and the interaction with the packing, rotor and casing (Cortes Garcia et al., 2017). An additional degree of freedom related to the rotation speed allows additional opportunities to fine-tune the design (Sørensen et al., 2014).

Models for HiGee and R-HiGee are not readily available in commercial simulation software. Nevertheless, Krishna et al. (2012) used the RadFrac module in Aspen Plus to perform rigorous rate-based calculations by discretising the R-HiGee unit into segments (differential annular rings). Then, all the segments were converted into a series of attached cylinders. The validation of results for a HiGee unit using this approach was satisfactory for a non-reactive separation. Then, a conventional RD was modelled and validated independently. Although the coupling of both models led to suitable and logical results, little application of the method is reported as the data provided is insufficient to validate the applicability, as noted by Hilpert et al. (2022). Other computer-aided tools applied in the study of R-HiGee are FORTRAN, Excel and COMSOL Multi-Physics (Gudena et al., 2012; Krishna et al., 2012).

Due to the complex interactions between hardware, operating conditions and the simultaneous phenomena, generic widely applicable models are out of reach (Illner et al., 2022), which hinders the integration of such process options into frameworks for process synthesis. According to Neumann et al. (2018), the industrial production of hypochlorous acid previously presented has reached a technology readiness level of 9, meaning that it is a proven technology. Nevertheless, no systematic design procedures exist to expand the application to other systems. Further research on R-HiGee packings is needed to provide higher residence times that could extend the applicability of this technology (Kiss et al., 2019), which could include the use of 3-D printed configurations for a rotor to help improve heat dissipation (Rao, 2022).

2.3.3 Catalytic cyclic distillation

Catalytic cyclic distillation (CCD) takes advantage of the functional and temporal domains of process intensification. While the functional domain exploits the synergy of simultaneous reaction and separation in a single column, the temporal domain introduces periodicity to the operation by creating a two-period cycle: vapour-flow period and liquid-flow period (Pătruț et al., 2014). To manipulate the duration of each period, CCD is fitted with special internals: plates containing the catalyst and trays with sluice chambers, as shown in Figure 2.3.

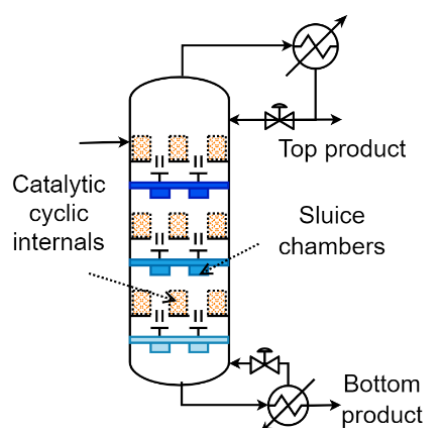


Figure 2.3. Schematic of catalytic cyclic distillation (adapted from Kiss and Maleta (2018) and Pătruț et al. (2014))

During the vapour-flow period, the liquid stays on the plates in contact with the catalyst, and the reaction takes place while the vapour passes up the column. Hence, the time available for reaction and the amount of liquid on a tray can be manipulated during the vapour flow period (Kiss et al., 2021). Kiss et al. (2019) indicate that the ability to control the duration of the vapour-flow period allows longer residence times and larger liquid holdups when compared with conventional reactive distillation operation, making CCD potentially suitable for relatively slow reactions. Then, the vapour flow stops during the liquid-flow period when the liquid travels from the tray to the sluice chamber. When another vapour-flow period begins, the sluice chamber opens, and the liquid flows to the empty tray below (Pătruț et al., 2014). Therefore, mixing between the liquid of different stages is avoided, which would otherwise lead to increased entropy – thermodynamic inefficiency – of the separation (Bîldea et al., 2016; Kiss and Maleta, 2018). The reduced fluid overflow results in less catalyst erosion, as Kiss et al. (2021) noted. A key limitation of CCD is that it cannot operate under a vacuum because of the pressure drop produced during the liquid flow period (Kiss et al., 2021).

Although cyclic operation at a commercial scale has been reported for stripping columns, rectification columns and dividing wall columns fitted with trays (Kiss et al., 2021), no CCD industrial applications have been disclosed in the open literature. However, a schematic of a cyclic distillation tray fitted with a catalyst has been provided by a technology vendor (Kiss and Maleta, 2018). Catalytic cyclic distillation has been investigated for the production of DME, MTBE and methyl acetate (Kiss et al., 2015; Pătruț et al., 2014; Rasmussen et al., 2022).

A rigorous model and simulation study for the production of DME by Pătruț et al. (2014) included mass and energy balances for each period and simplifying assumptions to facilitate their solution using numerical techniques implemented in equation solvers. The results

showed that CCD achieved higher purity than a conventional RD and used less vapour flowrate and fewer stages, which reduced energy consumption. To complement the model of Pătruț et al. (2014) that accounted for mass transfer only, Rasmussen et al. (2020) proposed a model that accounted for heat transfer too. The results of both studies presented similar trends for compositions, but temperature profiles differed. This difference is because the model that accounts for heat transfer considers temperature and composition variations during the vapour flow period. This analysis suggests that the modelling of CCD can take advantage of the additional degrees of freedom given by the duration of each period to achieve the desired results. In an effort to reduce the process complexity, Rasmussen et al. (2021) applied the previously proposed model in a well-known case study for the production of MTBE, where chemical equilibrium was assumed. They found that the cyclic operation positively affected the stage performance in the reactive section because of the reduced back mixing that improved the separation efficiency.

Rasmussen et al. (2022) proposed three quantitative metrics to evaluate the performance of CCD: Distance from equilibrium (meaning how fast chemical equilibrium is reached during the vapour flow period), the total production over a cycle, and the mean Damköhler number over a cycle. Perturbations evaluated are the duration of the vapour flow period, the vapour flowrate and the liquid holdup. The proposed indicators were applied to three case studies for the production of methyl acetate, MTBE and DME. In line with the earlier study from the same author, Rasmussen et al. (2021), it was found that the duration of the vapour flow period has a significant effect on the stage and column performance. In addition, it was suggested that the mean Damköhler number over a cycle could be a good indicator of the viability of CCD.

Simulation of cyclic distillation, both for the steady-state model and for the dynamic vapour flow periods, has been carried out in MATLAB (Rasmussen et al., 2021). However, commercial software for chemical process design cannot be adapted for simulating cyclic processes because the hydrodynamic limitations seen in operation are not reflected. This is because the embedded data about internals is not suited for cyclic distillation, as noted by Kiss and Maleta (2018). In addition, synthesis and design methodologies of dynamically intensified technologies face significant challenges regarding modelling, simulation and optimisation (Baldea and Edgar, 2018). Therefore, further research to develop methodologies for synthesis and conceptual design, simulation tools, control schemes, and optimisation is necessary to reach the industrial implementation of CCD.

2.3.4 Reactive heat-integrated distillation column

The reactive heat-integrated distillation column (R-HIDiC) exploits heat integration and process intensification by combining a heat-integrated distillation column (HIDiC) and a reactive distillation unit (RD) (Kiss et al., 2019; Vanaki and Eslamloueyan, 2012). The non-reactive HIDiC applies heat integration through the heat pump concept: energy is transferred from a rectifying section operating at higher pressure and temperature to a stripping section operating at lower pressure and temperature using mechanical work (e.g., compression) (Kiss and Ferreira, 2016). The rectifying section provides the heat required for vaporisation in the stripping section. For an R-HIDiC, a reactive section can be placed in either the stripping (Figure 2.4 a) or the rectifying (Figure 2.4 b) sections. The exothermic heat of reaction can partially supply vapour traffic inside the column (Figure 2.4 a), while endothermic reactions can help condensation in the rectifying section and generate more liquid reflux to the column (Figure 2.4 b) (Alcántara-Avila and Lee, 2016; Kiss et al., 2019; Vanaki and Eslamloueyan, 2012).

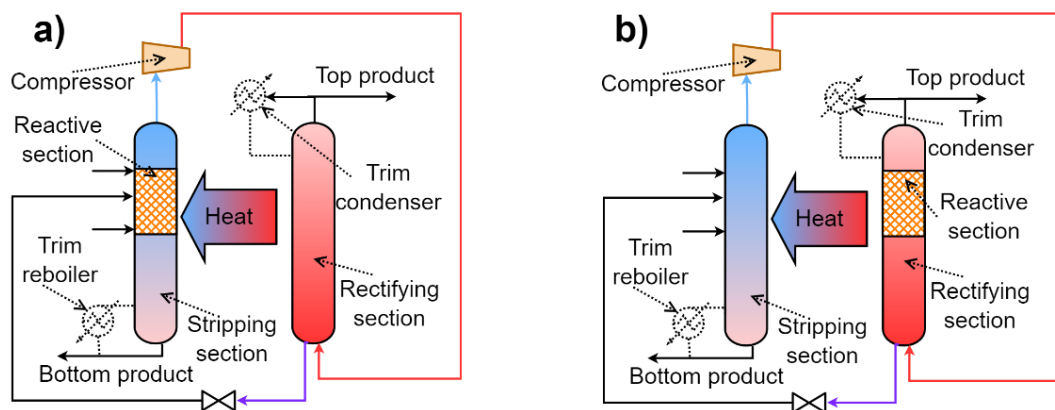


Figure 2.4. Schematic of R-HIDiC (adapted from Kiss et al. (2019))

A HIDiC without needing a condenser or reboiler is known as an ideal HIDiC. The heating and cooling required in this configuration are supplied by the rectifying and stripping sections, respectively, with a temperature driving force created by the shaft work of the compressor (Shahandeh et al., 2014; Suphanit, 2010). The partial HIDiC configuration contains a trim-reboiler or a trim-condenser, which supply any residual heating or cooling, respectively, and add flexibility to the operation, especially for start-up (Shahandeh et al., 2014; Smith, 2012). These definitions could be extended to R-HIDiC. Kiss and Olujić (2014) and Fang et al. (2019) provide review papers with extensive information about the working principles of HIDiC; modelling, simulation and optimisation; design and structural options; dynamics and control; and applications, which could provide insights for R-HIDiC.

The main advantage of R-HiDiC is that, as a result of the internal heat integration, demand for hot and cold utilities of the distillation column is reduced, which could be complemented by the heat of reaction. Thus, reboiler and condenser duties (and utility demand) can be reduced, leading to improved energy efficiency (Baldea, 2015; Kiss, 2013; J. Li et al., 2018; Varbanov, 2013). However, the need for a compressor can increase both electricity and capital costs (Vanaki and Eslamloueyan, 2012).

Unlike the industrial implementation of non-reactive HiDiC, commercially known as SuperHiDiC, by Toyo Engineering that has demonstrated energy savings (Toyo Engineering, 2019; Wakabayashi and Hasebe, 2015), R-HiDiC commercial applications are not known. Investigations of R-HiDiC include esterification and etherification reactions (Babaie and Nasr Esfahany, 2020; Pulido et al., 2011; Vanaki and Eslamloueyan, 2012) using heterogeneous catalysts.

Modelling of R-HiDiC follows the approaches for HiDiC, which assume either a uniform heat transfer area or a uniform heat load distribution (Gadalla, 2009; Suphanit, 2010). The design variables for R-HiDiC include the location of the reactive section, the number of rectifying and stripping stages, the feed location, the vapour fraction of the feed stream, the compression ratio (between the rectifying and stripping section), and the number of heat exchangers (Babaie and Nasr Esfahany, 2020), where the last two are the most important (Gutiérrez-Guerra et al., 2016). A small compression ratio between 1.3 and 3 (Kiss and Olujić, 2014; Suphanit, 2010) is preferred for economic operation because it helps to keep compression power demand low and is applicable for systems containing close boiling components, which could limit its application (Kiss, 2013). Regarding the number of heat exchangers, the SuperHiDiC concept can provide insights for design with a configuration with side heat exchangers allowing heat exchange between stages at different elevations (Wakabayashi and Hasebe, 2015), which can be applied to R-HiDiC.

Pulido et al. (2011) simulated an R-HiDiC using the RadFrac model in Aspen Plus. The model represents a concentric configuration, where energy exchange occurs through stage-to-stage interconnections. However, few details about the interconnections between stages and results were provided. Babaie and Nasr Esfahany (2020) presented an optimisation approach for the integrated operation of R-HiDiC in conjunction with pervaporation. The simulation of R-HiDiC was performed in Aspen Hysys. The optimised results showed a reduction of 29% in energy consumption when compared to RD operation. The optimal configuration required five

heat exchangers and one compressor, which increased the capital cost. However, the total annual cost (TAC) was reduced by 12% compared to RD despite the additional devices.

The commercial implementation of SuperHIDiC could lead to further development and industrial interest in R-HIDiC (Kiss et al., 2019). Nevertheless, design and control of R-HIDiC need further investigation due to the interactions between the vapour and liquid streams and the reaction involved in heat integration (Alcántara-Avila and Lee, 2016; Vanaki and Eslamloueyan, 2012). At the same time, optimising the operation of R-HIDiC, including economic estimations, is essential to evaluate the trade-off between energy savings and capital cost (Babaie and Nasr Esfahany, 2020). In addition, methodologies for simultaneous process synthesis and integration would help identify the potential of R-HIDiC during flowsheet development.

2.3.5 Membrane-assisted reactive distillation

In membrane-assisted reactive distillation (MA-RD), a membrane module is coupled to a reactive distillation column to aid separation, as the rate at which one species passes through the membrane is much larger than that of the other species. As a result of the coupled operation with reactive distillation, thermodynamic limitations (i.e., azeotropes) are overcome (Lutze and Gorak, 2013). The membrane module can be located after the distillate stream (Figure 2.5 a) or bottom stream (Figure 2.5 b) (Holtbruegge et al., 2014b; Lv et al., 2012).

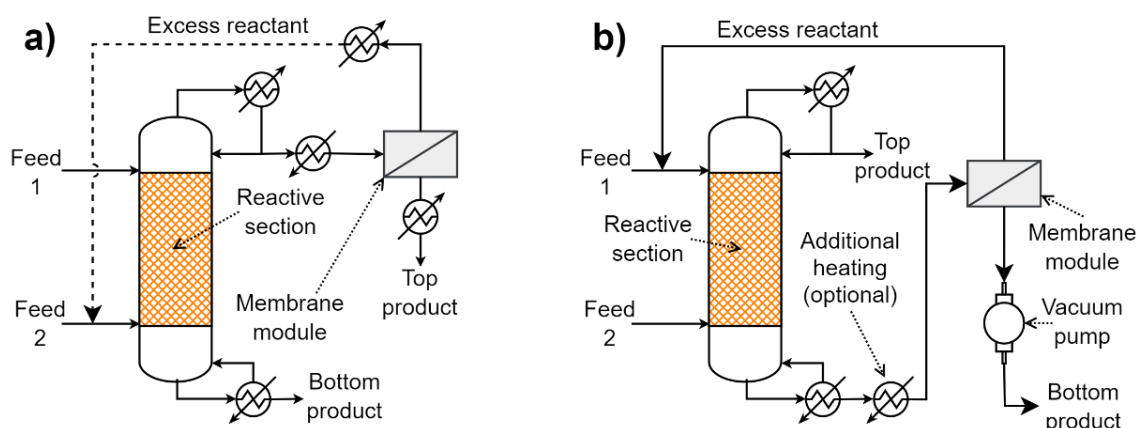


Figure 2.5. Membrane-assisted reactive distillation configurations a) vapour permeation in the distillate stream (adapted from Holtbruegge et al. (2014b)) b) pervaporation in the bottom stream (adapted from Lv et al. (2012))

Membrane separation methods typically applied to break azeotropes are vapour permeation or pervaporation, where the driving force is the difference in partial pressure (and difference in concentration for vapour permeation) (Wankat, 2012). Vapour permeation works with all

its streams in the vapour phase, so a vaporised inlet stream to the membrane is required, which may require additional heating (Figure 2.5 a). Unlike vapour permeation, the inlet stream to pervaporation is a liquid. The retentate exits the membrane module in a liquid state, and only the permeate is vaporised, aided by a vacuum system (Figure 2.5 b) (Holtbrügge and Pela, 2022). When using a homogeneous catalyst in reactive distillation, the membrane module can assist in the recovery of the catalyst to recycle it back to the reactive distillation unit, typically using nanofiltration as a membrane separation mechanism (Lutze and Gorak, 2013; Wankat, 2007).

Although industrial applications of membrane-assisted distillation focusing on azeotrope separation are reported (Liu et al., 2022), applications of MA-RD have been only investigated experimentally and in simulation (Holtbrügge and Pela, 2022). Vapour permeation and pervaporation assisting reactive distillation have been studied in a range of esterifications (Buchaly et al., 2007; Gudena et al., 2013a; Lv et al., 2012), transesterifications (Steinigeweg and Gmehling, 2004), etherification (Aiouache and Goto, 2003) and for the production of dimethyl carbonate and propylene glycol (Holtbruegge et al., 2014b; Li and Kiss, 2021).

For MA-RD, membrane modules and reactive distillation columns are modelled separately. Each model is either compared to the outcomes of other simulations or validated using laboratory or pilot-scale tests. The RadFrac module in Aspen Plus is commonly used to represent a reactive distillation column. Empirical and semi-empirical models usually describe physicochemical interactions between the components and the membrane, which can be implemented in Aspen Custom Modeller and as a User2 subroutine in Aspen Plus (Lutze and Gorak, 2013; Steinigeweg and Gmehling, 2004). However, membrane modelling and optimisation (including economics) are especially important during process design because of the high costs associated with the membrane module (Holtbruegge et al., 2012).

Scharzec et al. (2017) proposed a methodology for the synthesis and design of processes containing pervaporation units to determine their feasibility at an early stage. The degree of detail gradually increases, starting with ideal or generic models and building up to include economics. The methodology uses information about the pure components to evaluate the applicability of pervaporation using thermodynamic insights from the work of Jaksland et al. (1995), taking into account the solubility and molecular weight of the pure components as relevant properties for pervaporation. Then, residue curve maps are evaluated. When distillation boundaries exist, it is a good opportunity to apply hybrid operations to overcome

the distillation boundaries. Once sequences or combinations of operations are determined, shortcut and ideal models are used to minimise the energy use of the different configurations using NLP optimisation methods. Assuming there is potential for improvement in the proposed configurations, the next step consists of searching for a suitable membrane that serves the flux and compositions required. Finally, superstructure optimisation is used to minimise TAC after including sizing and costing equations. The optimisation uses ideal models for units that are not mature, (e.g., pervaporation), which is a common practice when applied at early stages.

While models and simulation tools for RD are quite mature (Shu et al., 2022), membrane modelling and design face challenges as the separation characteristics of membrane materials are studied for a given chemical system on a case-specific basis and require lab-scale experiments for validation (Holtbrügge and Pela, 2022). Therefore, generation of generic methods and model-based tools to enable membrane applications are heavily dependent on a precise molecular model to describe membrane separation and the integration with distillation, as noted by Liu et al. (2022). This limitation can be extended to reactive distillation.

2.3.6 Identified gaps, challenges and opportunities

Investigations and successful implementations of intensified technologies have shown that process intensification can substantially improve chemical processes. The literature on reactive distillation has highlighted several advantages and potential for future applications. Nevertheless, the limitations of reactive distillation are well recognised even at the synthesis and conceptual design level, particularly the need for the reaction and separations windows to overlap. It is proposed that some of the limitations preventing a broader application of reactive distillation can be overcome due to the additional intensification of advanced reactive distillation, thereby extending its applicability.

While a relatively small body of literature exists on how advanced reactive distillation technologies can be incorporated into a process flowsheet during the synthesis of a process, this literature review of advanced reactive distillation technologies reveals key characteristics of their configuration, advantages and disadvantages, industrial applications and research works, and modelling and design attempts focusing on them. Together with the analysis presented in section 2.2.4 regarding hybrid reaction-separation methods, it is evident that there is a lack of synthesis methodologies that consider advanced reactive distillation technologies.

Kiss and Smith (2020) have noted that one of the major challenges of adding reaction to the synthesis of integrated separation systems is the complexity introduced by the level of integration, complex dynamics and process control. This could be extended to advanced reactive distillation technologies due to the number of design degrees of freedom. Although advanced reactive distillation technologies show attractive prospects for industrial implementation, as noted by Kiss et al. (2019), their technical maturity is still low, which makes their implementation risky. The absence of industrial applications and scarce pilot tests results in the lack of ready-to-use models in commercial simulators. These challenges have led to the lack of validated design models.

Process simulation software supporting process development is still unavailable for advanced reactive distillation technologies. Nevertheless, the RadFrac model in Aspen Plus has been applied with some adaptations, as discussed individually for each technology. In other cases, proprietary models have been implemented in MATLAB or Aspen Custom Modeler, particularly for CCD and membranes. This makes reusing models or validation difficult, as only the results are typically provided and not the implemented models. Although advanced software covering simulation and optimisation of complex configurations, particularly for distillation applications, is available, it does not cover the additional intensification features such as cyclic operation, high-gravity fields, internally heat-integrated distillation, and reactions combined with dividing wall columns (Kiss and Smith, 2020). Table 2.1 summarises the identified gaps for each advanced reactive distillation technology, noting those that are addressed in this PhD thesis and detailed in the following chapters, as well as remaining challenges supporting future research perspectives discussed in Chapter 6.

In summary, modelling and simulation of advanced reactive distillation are inherently challenging due to the complexity of the systems, which need a deeper understanding of the underlying phenomena (Kiss et al., 2019). Also, the novelty of these technologies has prevented the development of commercial simulation tools for these 'niche' applications (Skiborowski, 2018). Therefore, there is still a need to derive a synthesis and design philosophy that provides a good starting point for introducing intensified technologies in the design of chemical processes. Thus, this PhD thesis aims to contribute to the progress of advanced reactive distillation technologies.

Table 2.1. Addressing gaps in the literature: PhD thesis contributions and remaining challenges

Technology	Gaps addressed in this PhD thesis	Remaining challenges
R-DWC	<ul style="list-style-type: none"> Heterogeneously catalysed reactions described by quasi-homogeneous models are typically considered, disregarding the occurrence of side reactions. The conceptual design of a dual R-DWC accounted for side reactions promoted by a reactive impurity and oligomerisation in the purification of lactic acid. Evaluation of systems with parallel reactions and multiple outlet streams. 	<ul style="list-style-type: none"> Dynamics and control are areas that require further research. There are uncertainties about the decomposition methods used in modelling and simulation. Experimental demonstrations are necessary to prove the concept and enable industrial implementation.
R-HiGee	<ul style="list-style-type: none"> Potential for industrial implementation is identified in systems with mass transfer limitations and fast kinetics. The synthesis methodology identifies 'relatively fast' reaction rates. The heat of reaction is evaluated in the methodology, considering heat transfer limitations. The methodology emphasises favourable conditions for systems with series reactions. 	<ul style="list-style-type: none"> Development of control strategies. Evaluation of mass transfer limitations due to the complex interactions between hardware, operating conditions and the simultaneous phenomena. Development of R-HiGee packing (i.e., 3-D printed configurations for a rotor) to provide higher residence times and improve heat dissipation.
CCD	<ul style="list-style-type: none"> CCD is favourable for systems featuring relatively slow reactions. The synthesis methodology identifies 'relatively slow' reaction rates. 	<ul style="list-style-type: none"> Development of simulation tools capable of evaluating dynamic operation, considering the effects of internals for cyclic operation on hydraulics. Development of methodologies for control schemes and optimisation.
R-HiDiC	<ul style="list-style-type: none"> Heuristics applied to non-reactive HiDiC for close-boiling components systems are extended for R-HiDiC. A procedure for building operating windows for the stripping and rectifying sections expands the range of operating conditions for separation and reaction. 	<ul style="list-style-type: none"> Models for HiGee and R-HiGee are not readily available in commercial simulation software Investigate design and control strategies due to the interactions between the vapour and liquid streams and the reaction involved in heat integration. Include economic estimations during optimisation to evaluate the trade-off between energy savings and capital cost.
MA-RD	<ul style="list-style-type: none"> Evaluation of systems with multiple outlet streams, particularly those containing azeotropes that are not consumed within the reactive section. The separation of such systems is facilitated by using the difference in partial pressures and concentrations as driving forces. 	<ul style="list-style-type: none"> Create general methods and tools for membrane modelling and design that can be applied to various chemical systems rather than being specific to a particular system. A thorough understanding of the membrane performance and the availability of membranes proven for real-industrial mixtures, compositions and conditions are needed.

2.4 Research questions

This literature review demonstrated that chemical process industries could be benefited from intensified technologies, such as advanced reactive distillation. Although significant progress is evidenced in research for the development of design methodologies accounting for intensified technologies, the questions that remain unanswered are:

1. Previous approaches for the design of reactive distillation and advanced reactive distillation technologies follow a technology-oriented approach without considering the overall process when designing new flowsheets. *How would one systematically synthesise an advanced reactive distillation technology and integrate its evaluation in a flowsheet during conceptual process design?*
2. Reactive distillation presents limitations principally regarding unfavourable volatilities, the need for overlapping operating windows and reduced flexibility for operation. Advanced reactive distillation technologies enable opportunities to expand the applicability of reactive distillation by exploiting additional intensification techniques and driving forces. However, these technologies have scarcely been evaluated in wide-scope methodologies. *What characteristics of the system can enable early-stage evaluation and help expand the applicability of reactive distillation by using advanced reactive distillation technologies, increasing its uptake as a processing option?*
3. Integration of functionalities in reaction-separation processes, particularly advanced reactive distillation technologies, results in complex interactions between phenomena where models to evaluate technical and economic performance are not proven. The lack of robust models and tools to evaluate advanced reactive distillation technologies has resulted in limited testing and few industrial applications. *What basis could allow the assessment of potential interactions between units and phenomena in order to define the operating region of an advanced reactive distillation technology in the early stage of process design?*
4. A number of advanced reactive distillation technologies have been investigated, but the reasons behind their selection have not been elucidated. *What tools could enable a quick and early-stage evaluation of advanced reactive distillation technologies, if any, to exploit a given chemical reaction and produce a desired product?*
5. Traditional and non-traditional chemical systems evaluated in reactive distillation have

been scarcely explored for application in advanced reactive distillation technologies.
What types of chemical systems are suitable for advanced reactive distillation technologies?

This thesis aims to answer the above research questions by developing a systematic methodology based on heuristics and first principles and introducing new concepts to develop process flowsheets accounting for advanced reactive distillation technologies that are usually overseen during the early stages of the design.

2.5 Concluding remarks

Whereas process synthesis and design have long been known as the pillars of process development, process intensification and the advent of novel technologies that integrate phenomena have created a new area for process development. Therefore, process synthesis, design and intensification support each other while pursuing interdependent objectives and outcomes.

Different approaches for process synthesis and design of intensified technologies, particularly conventional reactive distillation and hybrid reaction-separation, are presented, including heuristics-based, optimisation-based, and hybrid approaches. A discussion of the advantages and shortcomings of the approaches is provided.

With a focus on process intensification, particularly reactive distillation, this PhD thesis studies five advanced reactive distillation technologies that incorporate additional intensification techniques: reactive dividing-wall column (R-DWC), catalytic cyclic distillation (CCD), reactive internally heat-integrated distillation (R-HIDiC), reactive high-gravity distillation (R-HiGee), and membrane-assisted reactive distillation (MA-RD). Investigations and a few examples of applications are available in the literature. However, most of these studies follow a technology-oriented focus without considering a flowsheet, as demonstrated by the lack of methodologies for synthesis.

Finally, the identified gaps presented in the literature review are translated into research questions that are answered in the following chapters. The outcomes of this work aim to contribute to process design in chemical engineering by shifting away from considering only conventional unit operations and using novel technologies that exploit some of the benefits of process intensification.

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Chapter 3

Conceptual design of a dual reactive dividing wall column for downstream processing of lactic acid

3.1 Preface to Publication 1

Chapter 3 presents the first output of this research, Publication 1, its corresponding Supplementary Information, and a 'Perspective on Publication 1' section that highlights the findings and learnings from the conceptual design study. These learnings inform the research presented in later chapters. Publication 1 addresses Objective 2 of this PhD thesis:

2. To identify data, interdependent phenomena and constraints that could be expanded upon to create a generalised approach applicable to the synthesis of advanced reactive distillation technologies by developing a conceptual design of a dual R-DWC

Publication 1 illustrates how challenging and complex the conceptual process design of reactive distillation technologies is by exploring the conceptual design of a dual reactive-dividing wall column (R-DWC). This conceptual design is applied for the concentration and purification of biologically-produced lactic acid from a fermentation broth containing large amounts of water and succinic acid, an impurity. The dual-reactive dividing wall column contains two reactive sections where the forward reaction (towards products) and reverse reaction (towards reactants) occur separately. The forward reaction facilitates the separation of methyl lactate and heavier succinates, which are difficult to separate in their original acid form. The reverse reaction converts methyl lactate back into the acid form, free from the impurity. The simultaneous separation produces on-specification lactic acid.

Merging the reaction and separation tasks created a more compact flowsheet with a reduced number of units compared to published conventional configurations that include reactive distillation only. The evaluation, based on detailed process simulation, demonstrated the benefits of a dual R-DWC in terms of energy consumption, material intensity, water intensity and CO₂ emissions.

Publication 1 exposed some key characteristics of the process and the technology that need to be considered at the earliest stages of process design. The time-consuming and case-specific trial-and-error procedure of building a flowsheet with limited information and the limitations of models available in commercial simulations justifies the need for a structured and logical methodology for assessing the technical feasibility of advanced reactive distillation technologies. Understanding the potential effects of underlying phenomena in a complex system reveals process constraints (i.e., pressures and temperatures promoting thermal degradation) that need to be overcome.

3.2 Publication 1

Title: Conceptual design of a dual reactive dividing wall column for downstream processing of lactic acid

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Conceptual design of a dual reactive dividing wall column for downstream processing of lactic acid

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Highlights

- Novel dual reactive dividing wall column for processing bio-based lactic acid
- Methodology for synthesis and design of a dual reactive distillation column
- Advanced reactive distillation overcomes challenging separations (reactive impurities)

Abstract

Methodologies for designing intensified processing units are necessary to enable the industrial application of process intensification concepts. This article presents a ruled-based systematic methodology for the synthesis and conceptual design of a dual reactive dividing wall column (dual R-DWC). A decomposition approach is used to identify the tasks required for the separation by introducing a reactive separating agent to exploit a reversible reaction to enhance the driving forces. A combination of shortcut and rigorous simulations led to the conceptual design of a novel dual R-DWC in which the forward and reverse reactions, and the separation occur at once.

The methodology was demonstrated in a case study for the separation of lactic acid from dilute aqueous streams and a reactive impurity that hinders the lactic acid conversion and its recovery, while the byproducts may bring new challenges for the desired separations.

This study is the first to investigate the effect of reactive impurities on the reaction and the separation, hence adding a more realistic framework to the design. The flowsheet produced was evaluated against benchmark processes and showed a significant process improvement in terms of energy savings (ranging from 13–27 %), material intensity (28–32 % reduction), and water consumption (22–36 % reduction), while the reactive impurities are effectively removed.

Keywords: Process intensification; process design and simulation; process synthesis; reactive distillation

3.2.1 Introduction

The chemical industry faces increasing competitiveness and environmental regulatory constraints, which demand new approaches to improve different supply chain stages, process performance and operation mode. For example, the introduction of process intensification (PI) has been reported for various technologies and products, bringing significant benefits to the process without constraints limited to the unit-operation classical concept (Gorak and Stankiewicz, 2018). The application of PI to the design of chemical processes has demonstrated significant improvements in terms of efficiency, economics, safety and environmental performance due to the reduction of equipment size, energy consumption and waste formation (Moulijn and Stanckiewicz, 2017). One approach to incorporate PI in the design of chemical processes is combining functions leading to a synergistic effect that shows better process performance than the separate functions, i.e., reactive distillation (Stankiewicz et al., 2019). Reactive distillation (RD) exploits the synergy of the combined reaction and separation, which leads to benefits, such as separation improvement as the reaction overcomes azeotropes, and reaction improvement as the separation overcomes chemical equilibrium and enhances reaction rates, conversion and selectivity due to the constant removal of the reaction products (Kiss, 2017). Additional benefits arise when comparing the performance of RD with the conventional reactor-distillation sequence, such as capital and operating costs savings, less plant footprint, less recycling streams, and better environmental performance (Sundmacher and Kienle, 2003). Nevertheless, some constraints to RD's application need to be overcome. For example, specific ranges of temperatures and pressures must overlap, in addition to the limitations due to the thermal stability and the catalyst's life span (Orjuela et al., 2016).

Novel RD configurations with additional process intensification features (advanced reactive distillation technologies: R-DWC, R-HiGee, CCD, R-HiDiC, MA-RD) have attracted academic and industrial attention due to their potential to expand the applicability of RD. A survey, based on industrial and academic experience, qualitatively shows the degree of development of several advanced reactive distillation technologies in different aspects, including availability of methods and tools for design, simulation, dynamics and control as well as practical challenges (Kiss et al., 2019). Among them, the R-DWC presents greater development and ease of implementation, as extended benefits of the dividing wall column (DWC) applied for reactive systems, as described in a recent review paper about R-DWC (Weinfeld et al., 2018). Recent studies have also explored the use of pervaporation and pressure-swing reactive

distillation for systems containing azeotropes (Li et al., 2020; Li and Kiss, 2021; Wang et al., 2019). Beyond RD, dual RD has been demonstrated to exploit the synergistic thermodynamic features that lead to a compact and efficient multiproduct unit (Dimian et al., 2009).

Invited for the Special Issue on Advances in Bioprocess Intensification, this original paper focuses on expanding the applicability of reactive distillation by exploiting synergies through further intensification by combining a dividing wall and two reactive zones in one vessel, namely a novel dual reactive dividing wall column (dual R-DWC). The choice of using an R-DWC was a development from existing flowsheets that feature a sequence of reactive distillation columns, where the dual function (two reactive sections) is implemented under the same operating pressure following a rule-based approach. The dual function uses a reversible reaction to improve the driving forces and allows overcoming phenomenological limitations (high boiling points) of the initial separation through the forward reaction (Cardona Alzate et al., 2019). The reverse reaction is then used to recover the initial target molecules after the challenging separation has been accomplished. The reaction direction can be easily shifted by adjusting the liquid phase concentrations following Le Chatelier's principle. The application of the dual R-DWC can be evaluated for fluid chemical systems that feature multiple outlet process streams (products, impurities, excess water, mass separating agent) and the need for the forward and reverse reactions (e.g., esterification-hydrolysis). In principle, the methodology developed in this research can be applied to evaluate chemical systems that are suitable for RD, i.e., equilibrium-limited systems where the reactions take place in the liquid phase only. This research is demonstrated through a special case study where a reversible reaction is introduced to facilitate the initial separation problem: the purification of lactic acid (LA) from a dilute aqueous mixture with low-concentration impurities that exhibit similar physicochemical behaviour.

This paper is the first to carry out the synthesis and conceptual design of a process flowsheet based on an intensified dual R-DWC, which is at the centre of an industrial case study for the concentration and purification of a dilute aqueous stream of lactic acid (LA) from a fermentation broth. From a process design viewpoint, previous studies have overlooked the effects of impurities on the process performance, as process simulation research to date has not yet considered the effect of reactive impurities in the concentration of LA and used simplified fermentation broths, as detailed in section 3.2.2.4. Therefore, this investigation accounts for the impact of succinic acid (SA) as a heavy reactive impurity on the purification

of LA. The methodology follows a ruled-based approach that includes a synthesis procedure through a decomposition approach and the conceptual process design using shortcut models and rigorous simulations in Aspen Plus V8.8. Also, an energy integration analysis is performed to find additional opportunities for heat recovery. Finally, a brief assessment using process performance indicators is carried out, and the results are directly compared against the benchmark studies reported in previous articles.

3.2.2 Case study: Downstream processing of lactic acid

The application of a methodology to derive the intensified dual-reactive dividing wall column (dual R-DWC) is illustrated by a direct application to a case study. This section provides a general overview of lactic acid production, emphasising the last stages of preconcentration and purification along with the associated challenges, which are tackled by the proposed methodology. Also, the feed and product characteristics, the different approaches to handling impurities in lab-based and simulation-based studies, and the catalyst selection are addressed.

3.2.2.1 Lactic acid production process

Lactic acid (2-hydroxypropionic acid) is an α -hydroxy organic acid produced industrially for the first time through the chemical route in the United States. The chemical route limitations include high manufacturing costs and the inability to produce the desirable L-(+)-lactic acid stereoisomer (Datta and Henry, 2006). Figure 3.1 presents a block diagram of the conventional process for LA production. Most LA production processes are currently based on carbohydrate fermentation using microorganisms (Gruber et al., 2006). The microorganism's varying metabolism demand varying amounts and types of nutrients and produce fermentation byproducts such as fumaric acid, acetic acid, succinic acid, and ethanol. As a result, the fermentation broth constitutes a complex mixture because of the non-reacted sugars, excess nutrients and byproducts, determining the downstream processing steps (Oliveira et al., 2019). The possible configurations of LA downstream processing strongly depend on the fermentation broth composition and the purity required. Datta and Henry (2006) recognised that the separation and purification of LA remain the primary technology barriers due to the difficulty of removing salts formed during the fermentation stage, which poses a challenge to the final disposition options and generates an environmental liability.

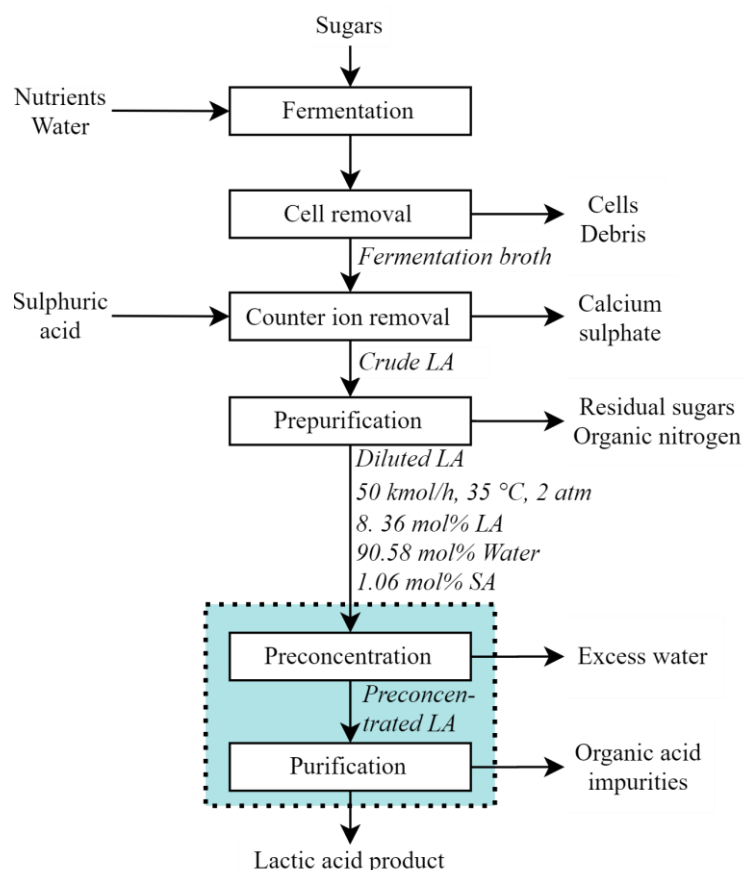


Figure 3.1. Process block diagram for conventional LA production. The dotted block includes the steps evaluated in this study (modified from Alves de Oliveira et al. (2018); López-Garzón and Straathof, (2014))

The dotted box in Figure 3.1 envelops the focus of this case study: the preconcentration and purification steps. The preconcentration stage removes the bulk solvent to reduce the solution's volume by evaporation in a range between 10 % to 75 % wt., while limiting the loss of lactate material from 0.1 % to 1 %wt. (Mizrahi et al., 2006). Finally, the purification stage removes the remaining organic acid impurities by reactive extraction, adsorption, electrodialysis and esterification, followed by reactive distillation. Among these purification techniques, RD can successfully separate other organic acids from LA while simultaneously removing excess water (Joglekar et al., 2006; Komesu et al., 2017a). The reaction of non-desired organic acids and alkyl alcohols into esters with different boiling points facilitates the separation via distillation (Qureshi et al., 2011). After the separation of the alkyl esters, the alkyl lactate hydrolyses back into the acid form. As a result, RD has been explored as a promising alternative to purify LA (Cho et al., 2008; Kim et al., 2017; Su et al., 2013). Yet, these studies assumed heavy impurities that are not reactive and thus easily removed, which is unrealistic. This study goes a step further by considering reactive impurities during the process synthesis and design.

3.2.2.2 Characteristics of the LA stream for the preconcentration stage

The composition of fermentation broths varies widely due to the type of carbon source, the pH, and the microorganisms used for fermentation. The typical concentration of lactate material in a fermentation broth varies between 8 to 15 % wt. (Mizrahi et al., 2006). The dilute acid mixture contains water, LA and other acids, including fumaric acid, formic acid, acetic acid, and succinic acid. For this investigation, a previously studied mixture containing succinic acid (SA) as an impurity (this time reactive) was selected to allow a fair comparison between conventional and intensified processes (Kim et al., 2017; Su et al., 2013).

3.2.2.3 LA product specifications

Among the group of organic acids, LA constitutes a versatile chemical with applications in cosmetics, foods, pharmaceuticals, and industrial use with mass concentrations of typically 50 %, 80 %, 88 % and 93 % (Gruber et al., 2006; Musashino, 2020). An emerging application of LA in the form of lactide monomers and co-monomers in concentrations of 100 % wt. is the production of polylactic acid (PLA), a bio-based plastic with promising applicability to replace fossil-based plastics (Okano et al., 2014). The major global producers of LA and derivatives are: Corbion Purac (The Netherlands), Galactic S.A. (Belgium), Henan Jindan Lactic Acid Co., Ltd. (China), Jungbunzlauer AG (Switzerland), Musashino Chemical Laboratory, Ltd. (Japan), and NatureWorks LLC (USA) (ReportLinker, 2020).

This research focuses on the production of LA 88 % wt. for the food industry, which is the most used industrially. The product specifications are LA 88 % wt., where dilactic acid (Di-LA) can be present up to 4.4 % wt., methyl lactate (ML) <1 % wt., and the remaining is water.

3.2.2.4 Reactive impurities

The separation of organic acids from LA is challenging due to the similar behaviour that these substances exhibit. The difference in boiling points cannot be easily exploited, as increasing the operating temperature may lead to thermal degradation. For these reasons, converting the acids into esters facilitates separation, as the boiling temperatures of the esters are lower than their corresponding organic acids. A literature survey about studies that evaluated LA purification revealed the contrasting approaches towards impurities and water content when performing experiments or process simulations. In general, lab-based experiments evaluated the purification of LA using either fermentation broths or synthetic mixtures that account for

impurities. In contrast, process simulation experiments use mixtures of LA and water only, in some cases also adding inert impurities.

Laube et al. (2016) studied the purification of LA experimentally from fermentation broths with impurities. As a result, a 15-unit operation process without reaction was produced, which did not effectively remove pyroglutamic acid, which is undesirable, especially for LA polymerisation into PLA. Uono (2013) focused on synthesising high-purity lactate from a solution that contained organic components as impurities. The author claims that salting out with acetone allowed the removal of impurities, but no values indicating the initial and final concentrations are provided. Khunnonkwao et al. (2012) studied LA's purification from a fermentation broth containing reactive acetic acid. This study focused mostly on membrane design, but there is no mention of the separation effectiveness. Benedict et al. (2006) carried out various tests for LA and SA's co-processing for ester production, evaluating catalyst and membrane suitability. The process used a batch catalytic reactor followed by a pervaporation-assisted distillation. However, the synthetic mixtures contained little or no water and a large excess of ethanol, which are not realistic conditions for industrial application.

The simulation-based studies focusing on the techno-economic evaluation of LA production dismissed the presence of impurities (Dai et al., 2018; Gasca-González et al., 2019; Komesu et al., 2015). Other researchers have focused on the preconcentration and purification of LA, and they have considered the presence of high-boiler components (SA, Di-LA, Tri-LA) that do not react and are easily removed (Cho et al., 2008; Kim et al., 2017; Su et al., 2013).

Additional studies about the separation of mixtures of organic acids that showed relevant results for this research include the work of Orjuela et al. (2011a), who studied, experimentally and in simulation, the separation of a mixture of succinic acid and acetic acid. This study showed the challenges and operating issues when dealing with the separation of organic acids. For example, the treatment of highly dilute mixtures (which resembled a fermentation broth) showed low conversion, so they were not evaluated further by simulation. In addition, the unreacted SA precipitated and obstructed the outlet line of the cooled bottom product. Boontawan (2012) studied a vapour permeation-assisted esterification of a mixture of acids containing formic acid, acetic acid and LA with ethanol. All acids were converted into esters and then separated in a conventional distillation column. While the experimental studies demonstrate that the esterification with alcohol is not selective of the target acid, the simulation studies tend to dismiss this fact by simplifying the model. These experiences

suggest that it is actually important to consider the impact of reactive impurities in the process performance. This study offers a more realistic approach by considering a heavy reactive impurity (succinic acid) as part of the LA feed to be purified in order to evaluate its impact.

3.2.2.5 Catalyst selection

Previous experimental studies about the esterification of LA have tested a range of cation exchange resins, including Amberlyst 15, Amberlyst XN-1010, D001, D002, and NKC (Benedict et al., 2006; Kumar et al., 2006; Sanz et al., 2004; Zhang et al., 2004). However, most kinetic studies have focused on the catalyst's characterisation, and not much attention has been paid to RD's operational constraints given by the device's mechanical and thermal limits. As a result, selecting a suitable catalyst is mostly guided by chemical performance only.

Amberlyst 15 is widely used for LA research in RD (Dai et al., 2018; Gasca-González et al., 2019; Kim et al., 2017; Su et al., 2013). For example, Su et al. (2013) set the maximum operating temperature of the catalyst of 120 °C as a constraint for the reactive section in an RD column. Indeed, this setting limits the operating window due to equipment constraints and hinders the reaction. To overcome this limitation, we introduced Amberlyst 36 as a solid/heterogeneous catalyst to give a broader range of operation up to 150 °C with a mass density of 800 kg/m³. This cationic resin catalyst exhibits a capacity of 5.40 eq/kg (i.e., the concentration of acid sites), while Amberlyst 15 presents a capacity of 4.70 eq/kg (Dupont, 2019). Therefore, this catalyst's performance can be considered at least as good as Amberlyst 15, and the kinetic data available is used in this work.

3.2.3 Modelling and simulation basis

This study uses a combination of equilibrium and rate-based models that account for the vapour-liquid equilibrium (VLE) and kinetics, respectively. The application of equilibrium and non-equilibrium models to describe R-DWC behaviour has been successfully validated against pilot-scale experimental data, which provides confidence in the approach followed in this investigation (Egger and Fieg, 2019). However, the availability of accurate vapour-liquid equilibrium (VLE) data and kinetics is somewhat limited. Therefore, the selection and validation of the property model data and kinetics are described hereafter.

3.2.3.1 Property model

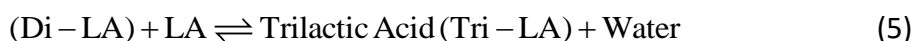
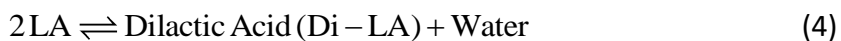
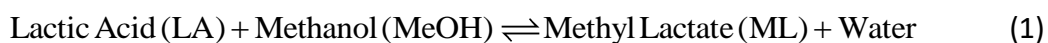
The property model needs to account for non-ideal behaviour and to handle consistently the phenomena associated with the presence of polar compounds (water, MeOH) and carboxylic

acids (LA and SA), such as the solvation and the dimerisation in the vapour phase of carboxylic acids. The UNIQUAC-HOC and NRTL-HOC property models are adequate for chemical systems that feature non-idealities and strong interactions between acids in the vapour phase. However, to avoid introducing new variables that may impact the comparison with the previously published benchmark studies, the UNIQUAC-HOC model was selected.

Only four pairs were gathered from built-in databanks in Aspen Plus v8.8, using experimental data from the Dortmund databanks (LA-Water, Water-MeOH, Water-SA, Water-ML), while the remaining pairs were estimated using the UNIFAC method in Aspen Plus. Therefore, proper model validation was carried out using experimental data available in the literature – this is presented in the Supplementary Information.

3.2.3.2 Chemistry and kinetics

In the present study, the concept of a '*reactive separating agent*' (RSA) is used for a compound to aid the separation through the reaction with the target component. This concept is analogous to the '*mass separating agent*' (MSA) and '*energy separating agent*' (ESA), which are used to aid separation by physical means only (Seider, 2017). Methanol (MeOH) was selected as the RSA based on the study of Su et al. (2013), which found that the MeOH system offered the lowest TAC as the flowsheet exhibited the fewest columns and produced the lightest lactate. In this manner, an equilibrium-limited and reversible reaction of the target components with an RSA could effectively remove impurities and recover the original purified compound through the reverse reaction. Consequently, the chemical system evaluated in this study consisted of eight components: the ones in the initial mixture and the reactions' products. Equations (1) to (5) illustrate the reactions included in the model.



The kinetic data for the esterification of LA with MeOH using Amberlyst 15 was obtained from the study of Sanz et al. (2004). The side reactions of SA with MeOH (Amberlyst 15) and the oligomerisation of LA (Dowex DR-2030) were gathered from the studies of Dudáš et al. (2014) and Asthana et al. (2006), respectively. A regression was applied to the experimental points

to calculate the kinetic parameters. When no data points were available for the reverse reaction, the chemical equilibrium constant was used to calculate the pre-exponential factor of the reverse reaction assuming that the activation energy is the same for both reactions. All the data sets were fitted to a pseudo-homogeneous kinetic model. The kinetic parameters for reactive distillation in Aspen Plus use a built-in power law expression, and the units depend on the basis selected for the holdup, which can be specified in terms of volume, mass or moles in the RadFrac module. The holdup basis selected in this study was the mass of catalyst per stage (which is 10 kg for esterification, and 12–14 kg for hydrolysis, assuming a catalyst occupancy of max 50 % of the holdup volume), so the corresponding units for the pre-exponential factor are expressed per mass of catalyst (e.g., $2.14 \cdot 10^4$ kmol/s·kg_{cat} for LA esterification) (Luyben, 2013). The catalyst bulk density (800 kg/m³) allows converting the pre-exponential factor into a catalyst volume-based unit (e.g., $1.712 \cdot 10^7$ kmol/s·m³). The details of each set of data and the calculated kinetic parameters are presented in Table 3.1.

Table 3.1. Kinetic models and parameters for the five reactions included in this study

Eq.	Reaction rate expression	Reaction type	Pre-exponential factor (kmol/kg _{cat} ·s)	Activation energy (kJ/kmol)
1	$r = m_{cat} (k_f a_{LA} a_{MOH} - k_r a_{ML} a_{water})$	LA esterification to ML	2.17e+04	48,733
		ML hydrolysis to LA	1.06e+03	48,487
2	$r = m_{cat} (k_f x_{SA} x_{MOH} - k_r x_{MMS} x_{water})$	SA esterification to MMS	1.10e+07	72,855
		MMS hydrolysis to SA	2.45e+05	72,855
3	$r = m_{cat} (k_f x_{MMS} x_{MOH} - k_r x_{DMS} x_{water})$	MMS esterification to DMS	4.40e+07	78,646
		DMS hydrolysis to MMS	5.57e+06	78,646
4	$r = m_{cat} (k_f x_{LA}^2 - k_r x_{Di-LA} x_{water})$	LA oligomerisation to Di-LA	2.00e+01	52,000
		Di-LA desoligomerisation to LA	9.99e+01	52,000
5	$r = m_{cat} (k_f x_{LA} x_{Di-LA} - k_r x_{Tri-LA} x_{water})$	Di-LA oligomerisation to Tri-LA	5.70e+00	50,800
		Tri-LA desoligomerisation to Di-LA	2.85e+01	50,800

r : rate of reaction (kmol/s), m_{cat} : catalyst mass (kg_{cat}), k_f : forward rate of reaction constant

(kmol/kg_{cat}·s), k_r : reverse rate of reaction constant (kmol/kg_{cat}·s), a_i : activity, x_i : mole fraction

3.2.4 Research approach

The synthesis and conceptual design of an intensified flowsheet followed a ruled-based approach (e.g., analysing boiling points to select operating pressure, composition in the liquid

phase) to drive the decisions to find opportunities for intensification and achieve performance improvement. The analysis and verification of each step of the synthesis and design used a combination of tools: a decomposition approach, shortcut calculations, rigorous simulation, and heat integration to achieve intermediate and final performance targets initially set in the scope of this conceptual design study. The assumptions of the proposed methodology include: no pressure drop across the columns, reaction in the liquid phase only, ideal mass transfer so an equilibrium model is used to describe mass transport between the liquid and vapour phases, kinetically controlled reaction described by a pseudo-homogenous kinetic model, reactive impurities that introduce additional components to the separation, fully-thermally coupled configuration equivalent to DWC (as negligible heat transfer occurs through the wall), and multiple outlet streams with one product stream on specification. The results allowed a better understanding of the process and an evaluation using a subset of sustainability metrics typically used during the early process design stages, such as material intensity, E-factor, energy intensity, water consumption and the associated CO₂ emissions (Argoti et al., 2019).

3.2.4.1 Decomposition approach applied to a dual reactive system

The decomposition approach was used to identify the individual tasks (functions) required for the reaction-separation problem: esterification, hydrolysis, rectifying and stripping. The esterification section carries out the forward reaction and converts LA and SA into their corresponding esters with lower boiling points. The stripping sections remove high-boiling components, while the rectifying sections drive the light components as overheads. Lastly, the hydrolysis section carries out the reverse reaction and converts the ML into LA. For this case study, the heaviest cut is removed in the first section of the arrangement, where the indirect sequence leads to a side-stripper configuration with a dual reactive function: esterification and hydrolysis. Then, these sections were coupled by placing the inlet, outlet and internal flows to drive the reactions (esterification or hydrolysis) and the separation, as shown in Figure 3.2. A detailed description of the approach applied to a dual reactive system is provided in the Supplementary Information (section 3.3).

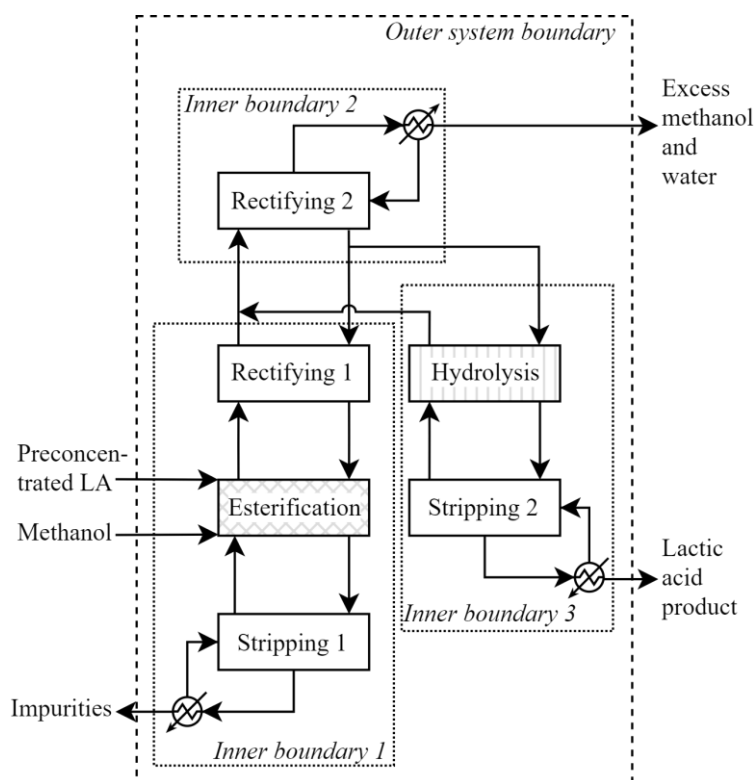


Figure 3.2. Sections and interconnections from the decomposition approach. The dotted and dashed boxes indicate the system boundaries for the shortcut calculations.

3.2.4.2 Shortcut calculation and initialisation values

The shortcut calculations consisted of mass balances applied around different system boundaries to obtain initialisation values for a rigorous simulation. The sections identified through the decomposition approach were grouped such that only one reaction lies within the boundary or a key degree of freedom can be calculated (e.g., liquid split ratio, reflux ratio, boilup ratio), as shown in the dotted and dashed boxes in Figure 3.2. The outer system boundary contained all sections and targeted the compositions of the top stream' containing MeOH and water and the product stream containing concentrated LA on specification. Next, three inner boundaries were considered around the esterification section, hydrolysis section and the rectifying section 2, where the latter featured the liquid split ratio at the top of the dividing wall that distributes the liquid between the two sections of the column (Yildirim et al., 2011). The composition of the liquid stream returning to the esterification section depends on the separation accomplished due to the VLE and the consumption and production rates on the second reactive section. Therefore, taking into account the reactions in the hydrolysis section to calculate the composition of the returning liquid stream constitutes an adaptation of the methods for designing a DWC and an R-DWC with one reactive section (Mueller et al., 2007; Triantafyllou and Smith, 1992). A detailed description of the shortcut calculations performed around the different boundaries of the system is presented in the Supplementary

Information (section 3.3). These shortcut calculations were fully automated in Excel, which facilitated recalculating values when accounting for non-sharp separations and partial conversion so that the operating parameters used to initialise the rigorous simulation account for a realistic system.

3.2.4.3 Rigorous simulation of the flowsheet and performance evaluation

Aspen Plus V8.8 was used to implement the flowsheet using the rigorous RadFrac module for the main units of the process. The process simulation results were used to calculate the key performance indicators and track various process variables.

Prior to implementing the novel dual reactive arrangement obtained from the decomposition approach, a preconcentration step was included to evaluate its performance in a full flowsheet. The preconcentration arrangement consisted of a heater, an expansion valve, and a flash vessel to promote an instantaneous separation of the feed into two phases: liquid and vapour. The flash vessel was set to operate adiabatically at atmospheric pressure (1 atm). The criterion to remove water in the preconcentrator followed two guidelines presented by Mizrahi et al. (2006): volume reduction from 10 % to 75 %wt., with a loss of LA between 0.1 to 1% wt. As the volume reduction allowed a wider variation range, only the LA loss was used as a design specification for the preconcentration arrangement, calculated with equation (6). Sensitivity analysis was used to evaluate the effect of the outlet temperature from the heater on the LA concentration and flowrate of the solution for further processing, and the LA loss.

$$\text{LA loss} = \frac{\text{LA mass flowrate in the vapour stream}}{\text{LA mass flowrate in the feed stream}} * 100 \quad (6)$$

The simulation of a dual R-DWC was performed using two RadFrac modules fully thermally coupled – a thermodynamically equivalent configuration, assuming that the mass-transfer resistances are equal and that the heat transfer through the wall is negligible (Novita et al., 2018). Figure 3.3 summarises the iterative procedure in a flowchart denoting four main activities: initialisation values adjustment, esterification column implementation, hydrolysis column implementation, and coupling. Several decision tasks within the main activity or to progress to the next activity checked simulation convergence and compliance with intermediate and final targets set for the individual and coupled performance of the columns. The shortcut calculations (previously described) provided the initialisation values for the operating parameters (e.g., reflux ratio, bottom-to-feed ratio, boilup ratio, bottom rate), heuristics provided initialisation values for the design parameters (e.g., number of stages, feed

location) and previous studies provided initialisation values for the catalyst holdup (e.g., 10 kg of catalyst per stage). The initial number of stages determined by heuristics was relatively large (30 stages per section: reactive, stripping, rectifying) (Al-Arfaj and Luyben, 2002). The feed streams to the esterification section were initially located at the two ends of the reactive section. Intermediate target values (e.g., conversion, desired split, target molecule losses) were set to fine-tune the number of stages following a sensitivity analysis procedure varying the catalyst holdup per stage, and the feed location and observing the temperature, composition and component generation profiles. Once the intermediate targets were met, the vapour stream leaving the esterification column was used as a feed stream to the hydrolysis column. The implementation of the hydrolysis column follows a similar initialisation procedure and fine-tuning until reaching the intermediate targets set (e.g., conversion, target molecule losses). Then, the returning stream leaving the hydrolysis section was updated in the esterification column following an iterative procedure until matching its composition and flowrate in the hydrolysis and esterification columns. Finally, the two columns were coupled and simulated to obtain the final target, which refers to the product specification. The Supplementary Information presents a detailed procedure to implement the dual R-DWC in Aspen Plus including the holdup variation, diameter sizing and convergence.



Figure 3.3. Methodology to implement a rigorous simulation of a fully-thermally coupled arrangement with two reactive sections (dashed connections considered after first iteration, yellow: initialisation values adjustment, green: esterification column implementation, red: hydrolysis column implementation, blue: coupling)

The distillate stream from the dual R-DWC contained excess water and MeOH, where the latter needs to be recovered and recycled, so an additional distillation column is employed. Finally, the recycle stream was connected to the esterification section, and the simulation was

satisfactorily run and converged. A detailed description of the implementation of the recovery column and the recycle stream is provided in the Supplementary Information.

Finally, the SPRINT software (v2.9), developed at the Centre for Process Integration (CPI) at the University of Manchester, was used to set energy targets and identify heat recovery opportunities (CPI, 2019). The mass and energy balances obtained from the rigorous simulation in Aspen Plus provided the stream data to be implemented in SPRINT. A minimum approach temperature of 10 K was selected, given the system's range of temperatures and the utilities included in the analysis (see Supplementary Information in section 3.3).

To complement the proposed flowsheet's technical evaluation, we assessed process performance indicators, a subset of sustainability metrics such as material intensity, E-factor, energy intensity, water consumption and CO₂ emissions typically used during the early process design stages based on mass and energy balances (Argoti et al., 2019). The use of sustainability metrics can guide improvements in operations by enabling the comparison with benchmark processes, tracking improvement over time, or evaluating alternative processes for the manufacture of a given product, where the lower the metric, the more effective the process (Schwarz et al., 2002).

The material intensity was calculated as the ratio of mass of input materials (including water only when it constitutes part of the product) minus the mass of product(s) over the mass of products (product and byproducts) (equation (7)). The E-factor accounts for the waste produced and it was calculated as the ratio of the mass of waste (excluding water) over the mass of product (equation (8)) (Sheldon, 2018).

$$\text{Mass Intensity} = \frac{\text{mass of raw materials in} - \text{mass of final product}}{\text{mass of final product}} \quad (7)$$

$$\text{E factor} = \frac{\text{total mass of waste}}{\text{mass of final product}} \quad (8)$$

The energy intensity was calculated using the overall heat duty of the reboilers and heaters over the mass of LA product. The water consumption metric comprises the volume of freshwater consumed in the process and the losses of water due to evaporation or disposal over the mass of LA product (equation (9)).

$$\text{Water consumption} = \frac{\text{fresh water inlet} + \text{losses from cooling} + \text{water disposed}}{\text{mass of final product}} \quad (9)$$

The CO₂ emissions associated with the preconcentration and purification steps were calculated based on the US-EPA-RULE-E9-5711 method, according to equation (10). This calculation considered the consumption of hot utilities only, assuming the use of natural gas as a fuel for steam production (so fossil fuel instead of renewable sources). The CO₂ emission factor is fuel-dependent and uses a default oxidation factor of one, which assumes that all the carbon present in the fuel oxidises. The CO₂ emission factor for natural gas is 5.589·10⁻⁸ kg CO₂/J. The energy source efficiency factor (*2006 IPCC Guidelines for National Greenhouse Gas Inventories*) assumes that the efficiency of the transformation of fuel to energy is higher than the efficiency of the transformation of fuel to electricity. The latter was not accounted for in the downstream section under study. Thus, for this research, the efficiency factor used is 0.85. The CO₂ emissions metric is presented as the mass of CO₂ over the mass of the LA product.

$$\text{CO}_2 \text{ emission rate} = \frac{\text{heat duty} * \text{CO}_2 \text{ emission factor}}{\text{energy source efficiency factor}} \quad (10)$$

3.2.5 Results and discussion

This section presents the results of each stage of the methodology and the analysis that drove the decisions made in the process synthesis and conceptual design journey. The results are organised as follows. Before the synthesis of potential processing options, the boiling points were analysed to select a suitable operating pressure. Then, a decomposition approach and the application of shortcut calculations informed the initialisation values to build a rigorous process flowsheet. Once a robust simulation offered the mass and energy balance results, the heat integration analysis and the process performance indicators were calculated and evaluated.

3.2.5.1 Boiling point analysis and selection of operating pressure

The components of the original mixture and the reactions' products were listed in increasing boiling points order. Table 3.2 presents the boiling and azeotrope temperatures at different pressures (see extended dataset in Supplementary Information in section 3.3). The maximum operating temperature for the reaction zone – limited by the thermal degradation of the catalyst (150 °C) – and the decomposition temperatures of the components were included as constraints. Also, the process design aimed to use cooling water as a cheap cold utility.

Table 3.2. Boiling temperatures of pure components and azeotropes at different pressures

Component Azeotrope*	0.1 atm		0.5 atm		1.0 atm		Decomp. Temp. (°C)
	Boiling point (°C)	Azeotrope composition (mol frac)	Boiling point (°C)	Azeotrope composition (mol frac)	Boiling point (°C)	Azeotrope composition (mol frac)	
MeOH	15.7	–	47.9	–	64.5	–	–
Water/DMS	45.7	0.96/0.4	80.8	0.95/0.05	98.9	0.95/0.05	–
					99.6	0.05/0.95	–
ML/water	46.0	0.02/0.98	81.4	0.04/0.96	99– 99.5***	0.05/0.95***	–
Water	46.1	–	81.7	–	100.0	–	–
ML	81.9	–	123.2	–	144.8	–	385**
LA/DMS	125.1	0.04/0.96	169.9	0.17/0.83	192.8	0.23/0.77	–
Di-LA/DMS	124.9	0.06/0.94	170.1	0.13/0.87	193.6	0.17/0.83	–
DMS/MMS	–	–	–	–	–	–	–
DMS	125.2	–	171.6	–	196.4	–	365**
Di-LA	150.6	–	193.7	–	215.9	–	–
LA/Di- LA/MMS	–	–	–	–	216.4	0.82/0.04/0.14	–
LA/MMS	154.6	0.48/0.52	195.5	0.73/0.27	216.4	0.83/0.17	–
LA	156.5	–	196.2	–	216.6	–	300
MMS	165.1	–	200.0	–	222.9	–	–
SA	244.5	–	292.5	–	317.6	–	235
Tri-LA	272.3	–	320.9	–	345.9	–	–

*All azeotropes are homogeneous

**Autoignition temperature

*** Experimental data (Chahal, 2000)

The reactive zone must contain the reactants in close contact to achieve the esterification between LA and MeOH, while ML needs to be recovered in the overheads after being separated from the heavier compounds. Pressures below atmospheric are preferred to drive the ML to the top without compromising the catalyst's integrity. LA and SA's decomposition temperatures limit the bottom streams' temperature, suggesting again to operate at low pressure. Clearly, a high vacuum favours the separation and avoids catalyst degradation, but lowered temperatures also hinder the reaction's progression (slow kinetics), and the top end of the column would require expensive cooling.

As the esterification reaction's purpose is to convert LA into ML, the first split aimed to produce an overhead product containing ML and lighter products, and a bottom stream of impurities, where ML and DMS were the light and heavy key components, respectively. However, azeotropes are possible between the two pure components. Thus, the temperature above the reactive section is required to be at least at the boiling point of ML, while the higher boiling azeotropes are maintained in the reactive zone to drive the reaction of LA into ML and push the heavier components downwards. The additional heat of the exothermic reactions

will raise the reactive section's temperature, so the temperature profile needs monitoring to avoid catalyst degradation in the lower end of the reactive section.

There is a compromise between the temperature to favour the separation and the reaction. Figure 3.4a presents ML, MMS and DMS's production rates at different temperatures assuming an equimolar feed, where temperatures below 193 °C favour ML production over MMS and DMS. Figure 3.4b presents ML, MMS and DMS's production rates at different pressures and evaluated at the corresponding boiling temperature of ML. This figure shows that increasing operating pressure raises the production rates of all products. However, the distribution favours MMS and DMS over ML, which will affect the consumption of MeOH. Thus, the operating pressure that favours the esterification of LA, while keeping low the production rates of MMS and DMS, was 0.5 atm.

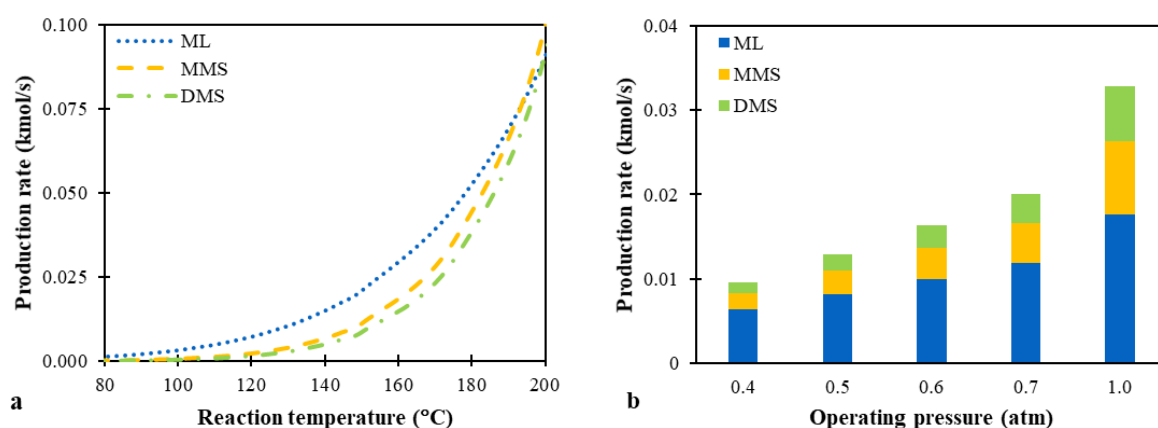


Figure 3.4. Production rate of the esterification products a) At different temperatures b) At different pressures at the boiling temperature of ML

3.2.5.2 Decomposition approach insight into shortcut models and rigorous simulation

The shortcut calculations over the boundaries depicted in Figure 3.2 provided the initialisation values for flowrates and compositions of the outlet streams and operating parameters set as specifications. The Supplementary Information (section 3.3) provides a block diagram and the shortcut calculations' results after evaluating a liquid split ratio of 0.4. Also, the bottom-to-feed molar ratio for inner boundary 1 was found to be $B/F=0.017$, and the reflux ratio for the inner boundary 3 was $RR=0.92$. These values are then used to initialise the rigorous simulation.

3.2.5.3 Rigorous simulation of the process flowsheet

3.2.5.3.1 Preconcentration of the fermentation broth

The sensitivity analysis (see Figure 3.5) evaluated the impact of the outlet stream temperature from the heater (manipulated variable) on the molar flowrate and the mass percentage of LA

of the liquid stream for further processing. The analysis indicates that temperatures lower than 127 °C allowed for maintaining the LA loss below the limit. A temperature of 126 °C was selected such that the LA loss corresponds to 0.69 % wt., and the flowrate reduction is approximately 40 %, which is in line with the specification suggested by Mizrahi et al. (2006). The vapour stream from the flash vessel contained mostly water with a low calorific value and provided heating, making use of the latent heat available, which is further discussed in the energy integration section 3.2.5.4. The liquid stream continued to the purification step.

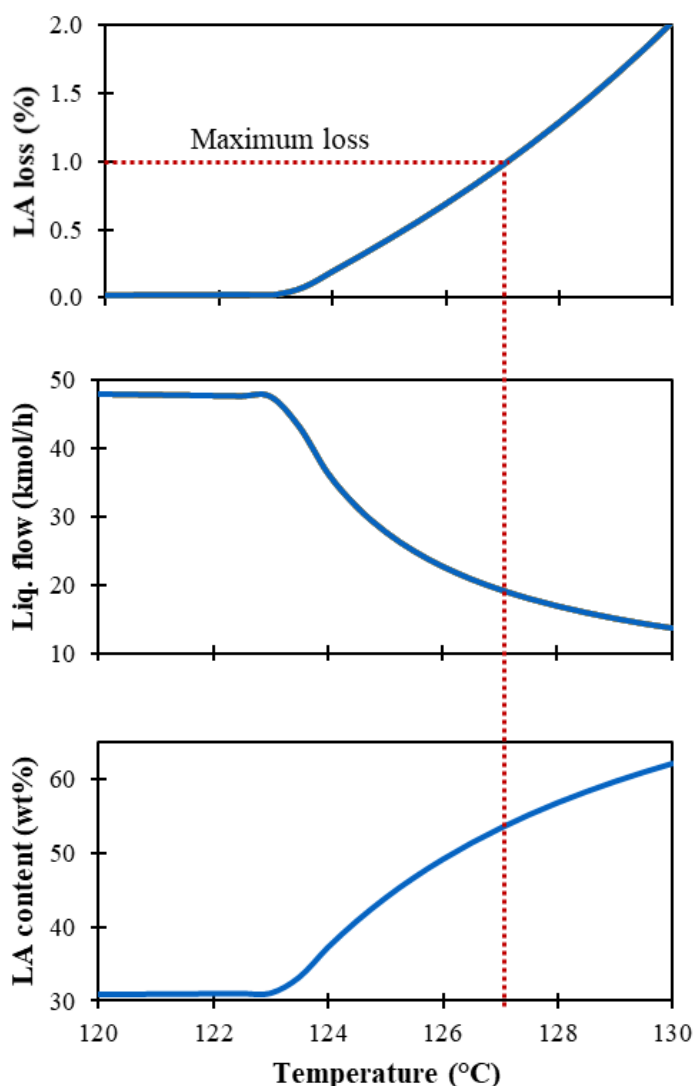


Figure 3.5. Sensitivity analysis of the effect of the heater outlet temperature in the preconcentration arrangement (The dotted line indicates the maximum LA loss allowed)

3.2.5.3.2 Dual esterification-hydrolysis dividing wall column and methanol recovery

Implementing a robust esterification column in Aspen Plus required additional setup parameters due to the complexity of the connections and interactions and new degrees of freedom. For example, the MeOH stream flowrate impacts the reaction and the reactive

section's temperature, which is constrained by the catalyst. With a stoichiometric feed ratio, the reaction zone temperatures were too high, which drove oligomers' high production rates. Thus, a sensitivity analysis was performed to find the MeOH-to-organic acids ratio that allows for maintaining the reaction zone at temperatures below 150 °C. Figure 3.6 presents the reactive section's column profiles resulting from the sensitivity analysis of the feed molar ratio of MeOH to the organic acids, LA and SA. Notably, the stoichiometric feed ratio of one led to temperatures of up to 350 °C, exceeding the catalyst constraint and promoting oligomers' production. Figure 3.6d shows Di-LA's production in the first reactive stages and then the consumption leading to Tri-LA production, which degrades the material and reduces the recovery, as the oligomers are removed with a high-boiling fraction containing the impurities. Increasing the MeOH-to-organic acids ratio clearly reduced the temperature along the reactive section and hindered oligomers' formation. Thus, the MeOH makeup is an important degree of freedom that plays a key role in maintaining the reactive section's temperature and the subsequent oligomer production. These results also support the selection of a catalyst that withstands higher operating temperatures. The production rate profile for ML in Figure 3.6c shows that the reverse reaction occurred in the first two reactive stages as the LA feed was rich in water and promoted the reverse reaction, with ML produced in the lower stages of the reactive section. Thus, moving the LA feed two stages above the reactive section allowed the reaction to occur from the first reactive stage, as some of the water fed was dragged to the top of the column. Increasing the MeOH concentration in the liquid phase with increasing molar feed ratio favoured the esterification reaction, as presented in Figure 3.6b.

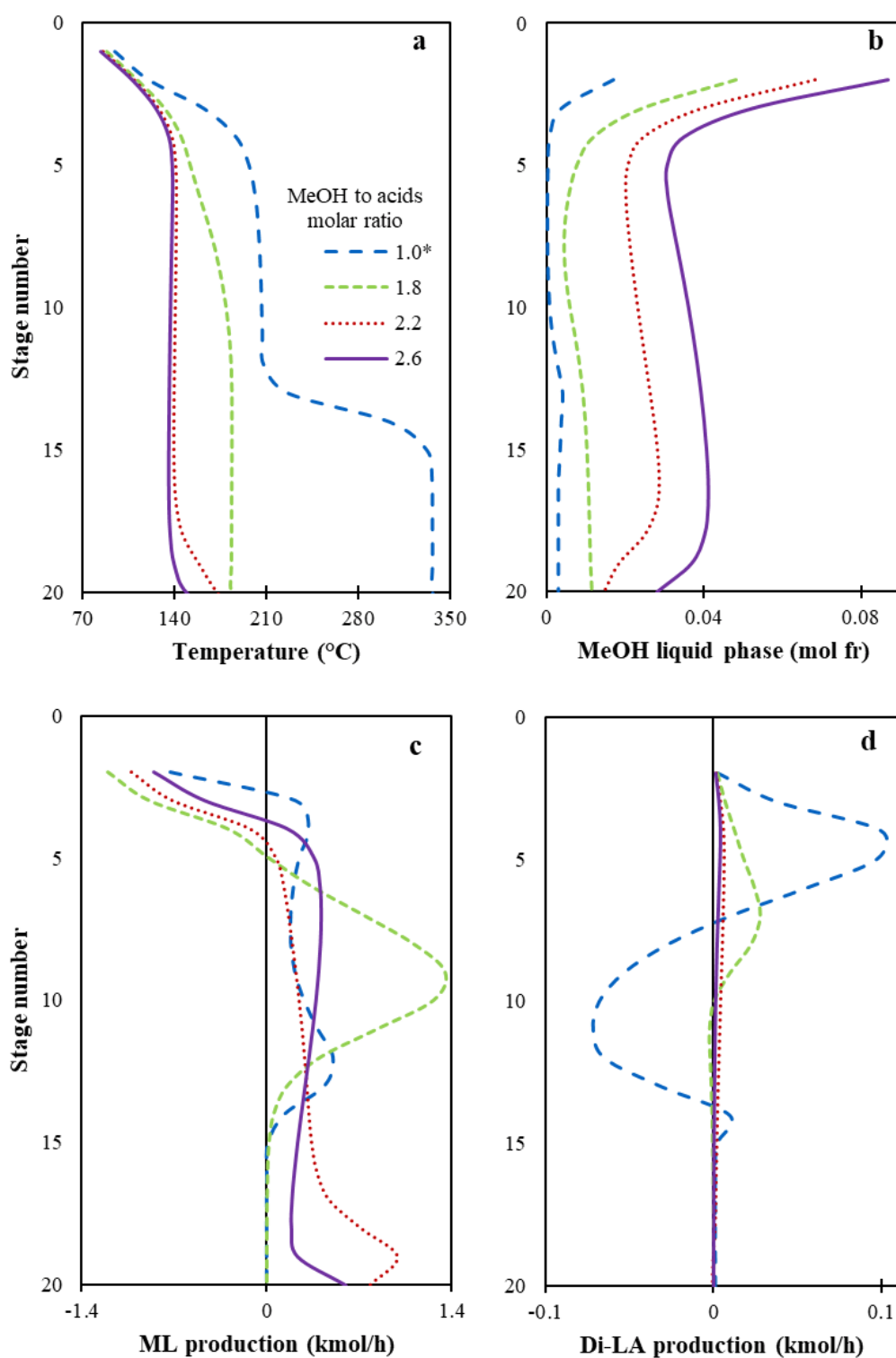


Figure 3.6. Column profiles for the esterification section (*stoichiometric ratio)

The condenser was removed once a relatively constant temperature along the reactive section is obtained by simulation. Then, a new degree of freedom must be considered: the liquid split ratio that dictates the incoming liquid stream required in the column. The returning stream composition was set using the information from the shortcut calculations, and the flowrate was evaluated in a sensitivity analysis with different split ratios, presented in Figure 3.7.

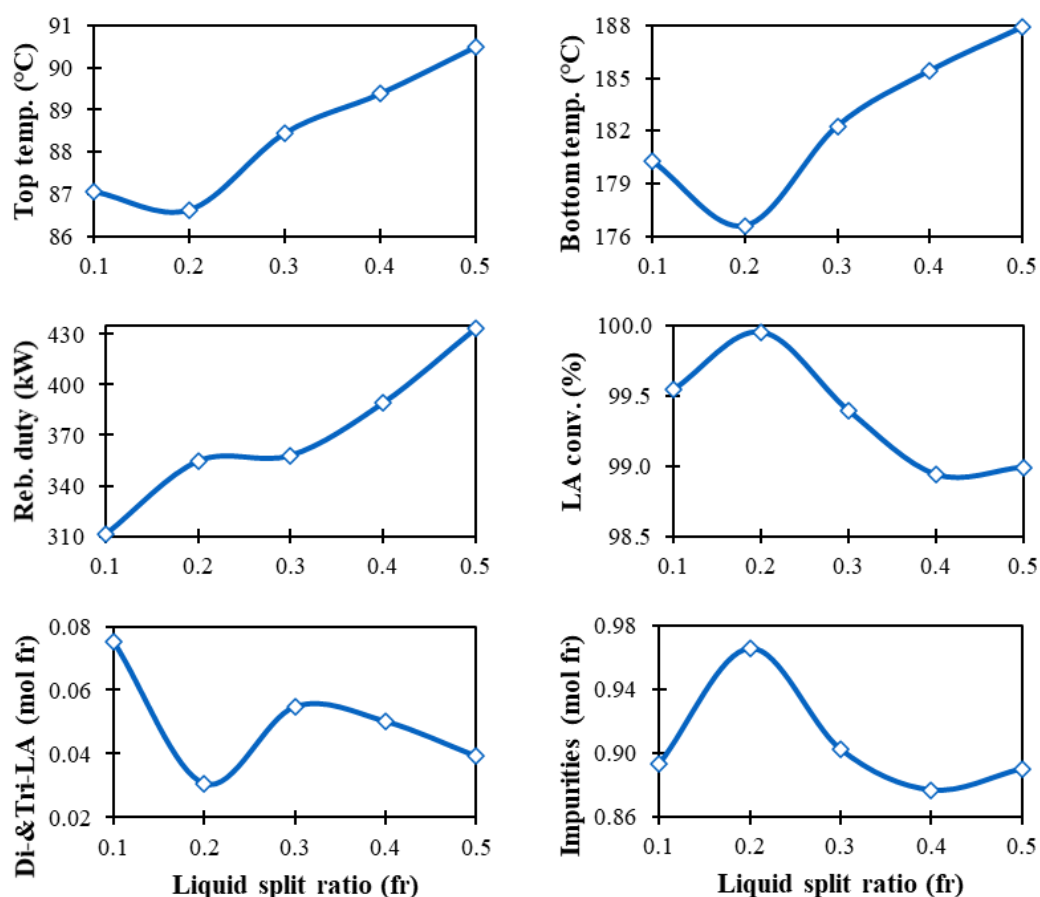


Figure 3.7. Sensitivity analysis of the effect of liquid split ratio on the esterification section

As a result, the higher the split towards the esterification section, the higher the reboiler duty due to the increased volume returned. However, the remaining parameters showed a minimum temperature (top and bottom) and Di-&Tri-LA molar fraction; and a maximum conversion and impurities removal using a split ratio of 0.2, which is used to build a base case. Small discrepancies are attributed to the adjustment needed in the manipulable operating parameter (bottom-to-feed ratio) to align with the mass balance and subsequent convergence. Therefore, a liquid split ratio of 0.2 towards the esterification column was selected to continue building the simulation. Further optimisation of the liquid split ratio could be explored in the vicinity of this value following a multi-objective optimisation procedure beyond the conceptual design in the scope of the proposed methodology. The Supplementary Information (section 3.3) presents detailed information on the setup parameters and results to obtain a robust esterification column simulation.

The implementation of the hydrolysis column in a RadFrac module used the initialisation values from the shortcut calculations and simulation results from the esterification column. Figure 3.8 shows the profiles of the composition of the liquid phase and the production rates

per stage. The analysis of both profiles is quite revealing in several ways. First, in Figure 3.8a, it is evident that most ML, once fed, travelled upwards without contacting the catalyst. Second, the high ML concentration compared to the MeOH concentration above the reactive section is also indicated by the low hydrolysis reaction rates. In addition, the concentration of water in the liquid phase, which is not depicted, was sufficiently high to guarantee the reaction's occurrence. Thus, the inlet and returning stream locations were systematically lowered in the reactive section so that the ML conversion improves and the ML loss in both ends of the column is reduced. Nevertheless, a compromise should be made between the increase in conversion and the ML concentration in the bottom stream; as the feed stream moves downwards, the bottom stream is also enriched in this component. Figure 3.8c shows the improved case where the number of reactive and stripping stages and the catalyst holdup have been adjusted.

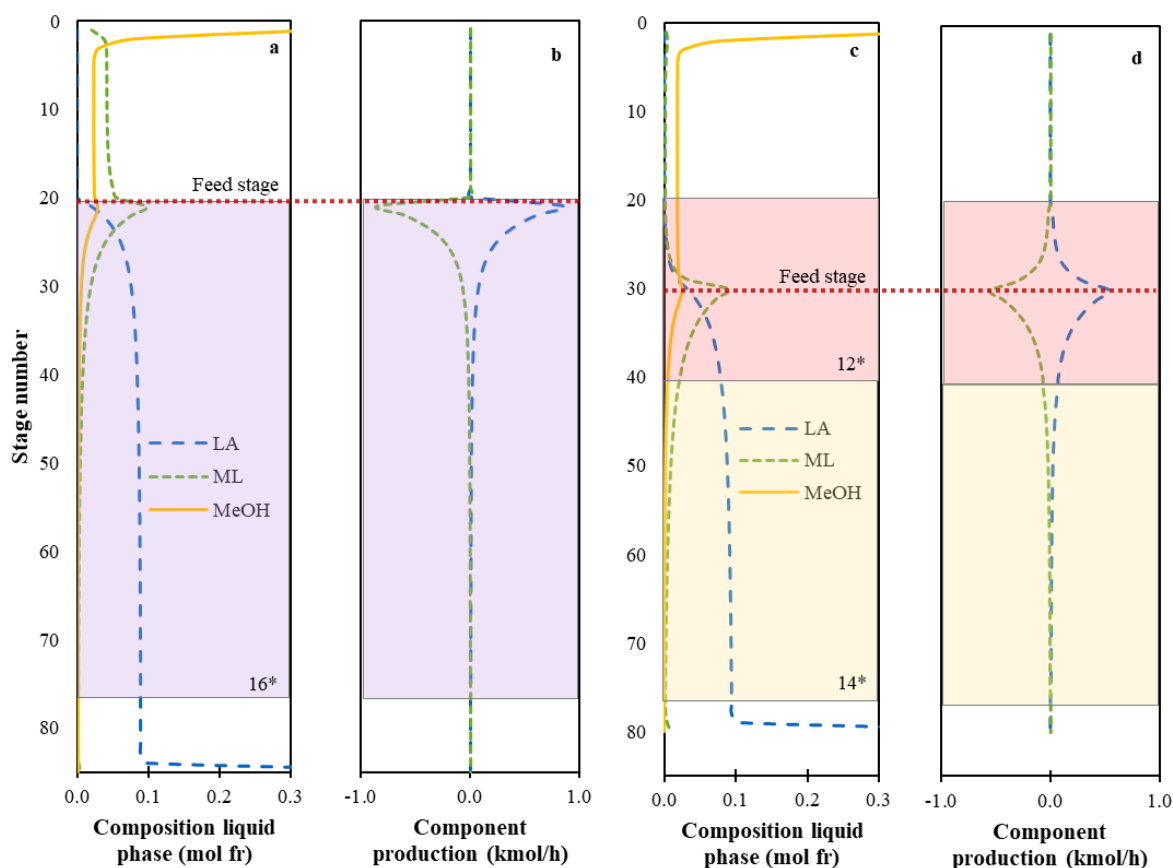


Figure 3.8. Column profiles for the hydrolysis column with the shaded region representing the reactive section (*mass of catalyst per stage in kg)

Coupling the esterification and hydrolysis columns in Aspen Plus required several iterations until reaching the targets set for each column's operation and the product specifications, as described in the flowchart of Figure 3.3. The final step to complete the simulation of the dual R-DWC required the implementation of the recycle stream after the simulation of the recovery

unit. Table 3.3 provides details about the setup parameters for esterification and hydrolysis columns, and the intermediate and final targets for the base case (before coupling), thermally coupled columns after integration and the configuration including the recycle stream. The iterations that led to significant changes in the parameters occurred when coupling both columns. Then, once the recycle stream was calculated and implemented, the MeOH makeup flowrate was the one that required substantial adjustment, which was defined by the design specification to keep the reactive section at $< 150\text{ }^{\circ}\text{C}$. The intermediate targets defined for the esterification section included LA conversion $> 99\%$, near-sharp ML-DMS split and LA loss $< 1\%$. The LA conversion and ML-DMS split were easily achieved. The LA loss in the bottom stream was reduced with the adjustments carried out in the number of stages and feed location. For the hydrolysis section, the intermediate targets included ML conversion $> 80\%$ and ML loss in the top and bottom streams $< 2\%$. The base case presented a low conversion of methyl lactate as some material exits the column to enter the esterification section. Once coupled, the location of the inlet and side-draw streams and the catalyst holdup adjustment allowed reaching higher conversion and reduced the loss of ML from both ends of the hydrolysis section.

Table 3.3. Setup parameters and key results tracked to simulate a dual R-DWC

Description	Units	Base Case	Fully thermally coupled	Fully thermally + recycle
Setup parameters esterification column				
Number of stages		29	25	25
Specified bottom-to-feed ratio		0.020	0.015	0.015
Number of rectification stages		4	8	8
Number of reactive stages		20	12	12
Number of stripping stages		5	5	5
Catalyst mass per stage	kg	10.0	10.0	10.0
Feed lactic acid stage		3	6	6
Feed methanol stage		24	20	20
Setup parameters hydrolysis column				
Number of stages		85	85	85
Specified bottoms rate	kmol/h	6.2	6.6	6.6
Specified boilup ratio		5.5	5.5	5.5
Number of rectification stages		20	10	10
Number of reactive stages		45	30	30
Number of stripping stages		20	45	45
Catalyst mass per stage	kg	16	12, 14	12, 14
Methanol makeup flowrate*	kmol/h	4.828	9.295	0.813
Results esterification column				
Equipment related results				
Temperature top stage	°C	85.6	83.0	83.0
Temperature bottom stage	°C	178.9	182.2	183.1
Reboiler duty	kW	344.7	432.6	426.6
Stream results				
Preconcentrated LA (Feed to C1)	kmol/h	19.269	22.654	22.654
LA	kmol/h	4.140	4.152	4.152
Water	kmol/h	14.598	17.971	17.971
Vapour stream from C1	kmol/h	30.521	38.397	38.514
MeOH	kmol/h	4.245	8.696	8.778
Water	kmol/h	21.768	25.239	25.276
ML	kmol/h	4.507	4.461	4.459
Liquid returning stream to top of C1	kmol/h	2.780	2.780	2.780
MeOH	kmol/h	0.116	0.118	0.119
Water	kmol/h	2.236	2.332	2.332
ML	kmol/h	0.428	0.250	0.250
Impurities from C1	kmol/h	0.566	0.542	0.544
Di-LA	kmol/h	0.026	0.008	0.008
SA	kmol/h	0.061	0.124	0.128
MMS	kmol/h	0.289	0.239	0.224
DMS	kmol/h	0.180	0.168	0.179

Table 3.3. Setup parameters and key results tracked to simulate a dual R-DWC (continued)

Description	Units	Base Case	Fully thermally coupled	Fully thermally + recycle
Intermediate esterification targets				
ML top split fraction		1.000	1.000	1.000
DMS bottom split fraction		0.999	1.000	1.000
LA conversion	%	99.77	99.93	99.88
LA lost in C1	%	1.48	0.48	0.53
Impurities molar fraction (DMS+MMS+SA)	mol fr	0.94	0.98	0.98
Results hydrolysis column				
Equipment related results				
Temperature top stage	°C	59.5	57.6	57.6
Temperature bottom stage	°C	101.8	106.9	106.9
Condenser duty	kW	635.2	888.1	889.3
Reboiler duty	kW	280.5	447.8	447.8
Reflux ratio	molar	1.671	1.703	1.696
Stream results				
Vapour stream from C1 (Feed to C2)	kmol/h	30.521	38.397	38.514
MeOH	kmol/h	4.245	8.696	8.778
Water	kmol/h	21.768	25.239	25.276
ML	kmol/h	4.507	4.461	4.459
Side-draw from C2	kmol/h	2.780	2.780	2.780
MeOH	kmol/h	0.116	0.118	0.119
Water	kmol/h	2.236	2.332	2.332
ML	kmol/h	0.428	0.250	0.250
LA product	kmol/h	6.960	6.618	6.618
LA	kmol/h	3.601	4.003	4.001
Di-LA	kmol/h	0.013	0.009	0.009
Water	kmol/h	3.249	2.578	2.579
ML	kmol/h	0.096	0.028	0.028
Excess MeOH and water from C2	kmol/h	20.781	28.999	29.116
MeOH	kmol/h	7.758	12.679	12.758
Water	kmol/h	12.668	16.237	16.275
ML	kmol/h	0.355	0.082	0.082
Intermediate hydrolysis targets				
Methyl lactate conversion	%	88.94	97.38	97.38
LA lost as ML (top)	%	8.57	1.98	1.98
LA lost as ML (bottom)	%	2.32	0.68	0.68
Final targets				
LA product	kg/h	395.120	411.463	411.329
LA+Di-LA	wt fr	0.826	0.880	0.880
Water	wt fr	0.148	0.113	0.113
ML	wt fr	0.025	0.007	0.007
Purification section LA recovery	%	86.98	96.41	96.37
Overall LA recovery	%	86.11	95.72	95.67

*Defined by the design specification over the temperature in the reactive section

3.2.5.3.3 Mass balance and key parameters

Figure 3.9 presents the process flowsheet for the preconcentration and purification of LA, and the key stream-data and design features. First, the dilute LA entered a flash vessel (V-1) arrangement, including a heater and a valve. The water-rich vapour stream provided low-grade heat to be recovered, while the preconcentrated LA liquid stream entered the esterification column (C-1). The impurities were removed in the bottom stream of C-1. The ML-rich stream was then fed to the reactive section in the hydrolysis column (C-2) while a liquid side-draw entered the top of C-1. The LA product was removed from the bottom of C-2. The distillate stream from C-2 entered a distillation column (C-3) to remove excess water and recover MeOH.

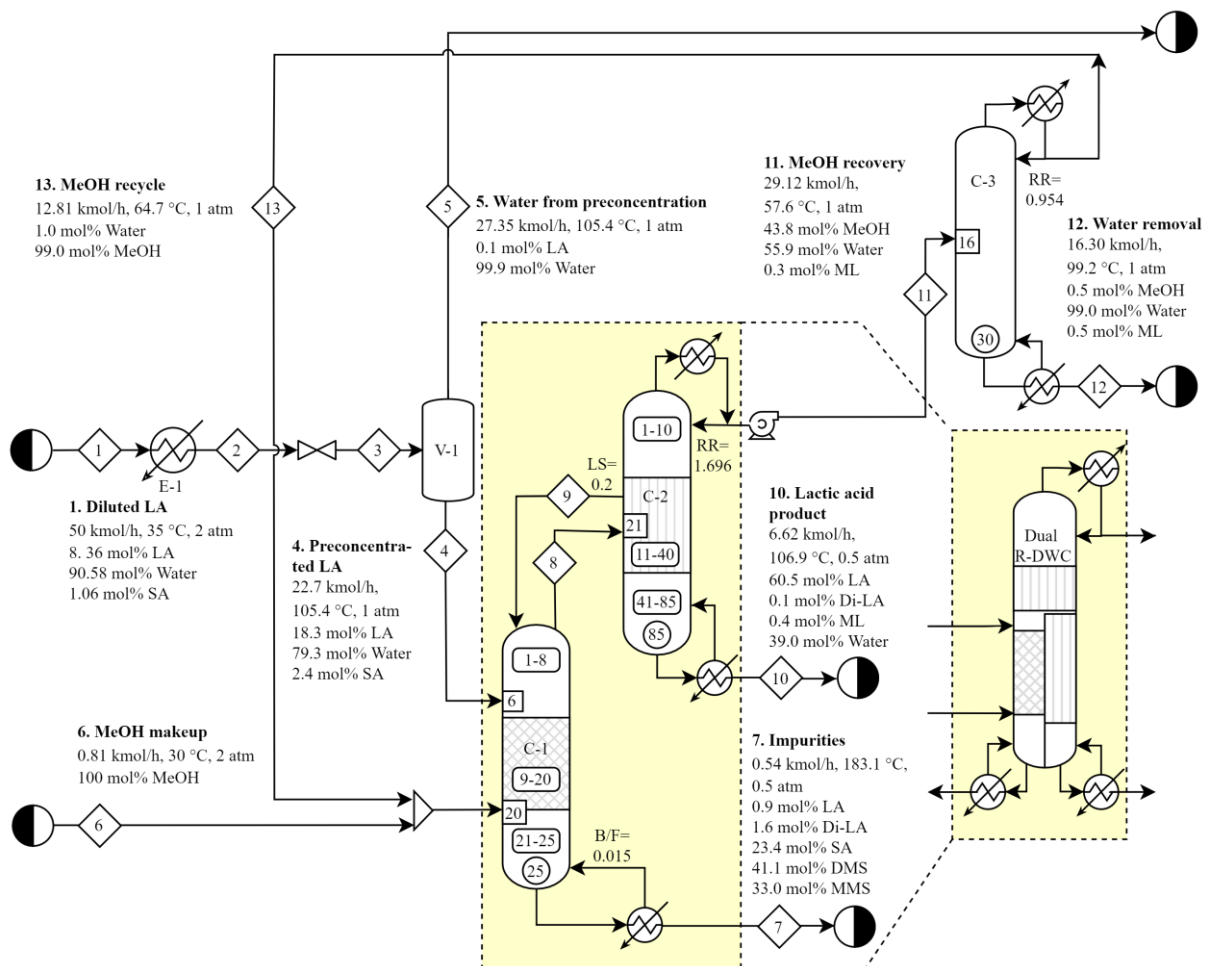


Figure 3.9. Process flowsheet and key stream data for the preconcentration and purification of LA. The dashed box presents the fully-thermally coupled arrangement equivalent to a dual R-DWC (◇ stream number, □ inlet stage, ○ total number of stages, ▭ stages per section, B/F bottom-to-feed molar ratio, RR reflux ratio, LS liquid split ratio)

3.2.5.4 Heat integration of the flowsheet

Figure 3.10 presents the composite curves of the process, where the blue curve represents the cold composite curve, and the red curve represents the hot composite curve. The overlap between the two curves denotes that the heat available for process-to-process recovery was 267.7 kW, which resulted in a reduction of hot and cold utilities of 17 % and 22 %, respectively. The minimum cold utility (cooling water) corresponds to 1177.3 kW, and the minimum hot utility accounts for 1280.3 kW (distributed in 853.3 kW of low-pressure steam and 427 kW of high-pressure steam). The initial conditions and design constrain the heat recovery (e.g., feed condition for downstream, flash vessel pressure). However, the flash vessel pressure selected could bring the benefits of reducing capital and operating costs due to using standard operating conditions.

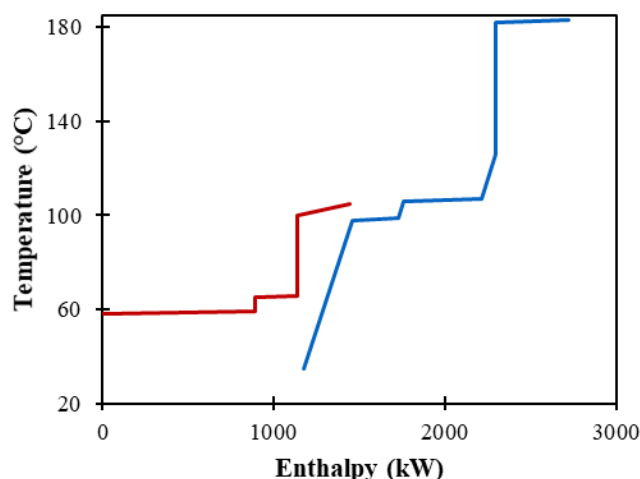


Figure 3.10. Composite curves of the process

3.2.5.5 Process performance indicators: A subset of sustainability metrics

The process's sustainability was evaluated using process performance indicators based on mass and energy balances proposed by industrial experts: material intensity, E-factor, energy intensity, water consumption, and CO₂ emissions. These values allow comparing the operations performance with benchmark processes, with lower values meaning better performance.

3.2.5.5.1 Material intensity

This metric indicates the input materials used per unit of output. The inlet streams to the process are LA in the dilute feed = 376.6 kg LA/h, SA in the dilute feed = 62.7 kg SA/h, the MeOH makeup = 26.1 kg MeOH/h and the water fed that is intended to be part of the product (12 % wt.) that corresponds to 51.4 kg water/h ($376.6 \times 12 / 88$), and the product (output)

corresponds to 411.3 kg/h of LA (88 % wt.). The impurities stream is a mixture of SA, MMS and DMS that is not considered a co-product. As a result, the material intensity of the proposed flowsheet is 0.256 kg_{input}/kg LA product. Note that the calculation of material intensity for the benchmark studies (section 3.2.5.6) featured an additional input: the water used for the hydrolysis of methyl lactate accounted stoichiometrically, and the implications will be discussed accordingly.

3.2.5.5.2 E-factor

The E-factor gives an indication of the waste produced in the process. The waste stream corresponds to the impurities containing SA and its corresponding esters, MMS and DMS, and is equal to 73.3 kg/h. The E-factor for the proposed flowsheet is 0.178 kg_{waste}/kg LA. It is important to note that by considering the SA as a reactive impurity, the esters produced have a higher molecular weight and consume part of the MeOH fed to the process. To reduce the waste produced, the impurities stream could be upgraded into DMS for applications such as flavouring agent, paint additive, pigment solvent and viscosity adjustor (Seqens, 2021).

3.2.5.5.3 Energy intensity

Energy intensity is a measure of the primary energy consumed per unit of output, considering the heat duty of reboilers and heaters. The energy intensity for the process proposed here is 13.5 MJ/kg LA product before indirect heat integration (base case) and 11.2 MJ/kg LA product (including heat recovery).

3.2.5.5.4 Water consumption

This metric indicates the freshwater consumed per unit output, which accounts for the freshwater inlet, losses from cooling, and water disposal. One of the major realisations of the proposed flowsheet was the reuse of the water produced in the esterification section to carry out the hydrolysis reaction. Therefore, no additional freshwater was introduced to the system. The evaporation losses were estimated as 7 % of the cooling water (Schwarz et al., 2002). The cooling water flowrate was computed from the cooling duty once heat integration was introduced (1135.2 kW), and the cooling capacity of water was 20.9 kJ/kg given by the supply and return temperatures of cooling water, 25 °C to 30 °C. Therefore, the loss by evaporation of cooling water corresponds to 13.7 m³/h. The proposed flowsheet features two outlet water streams containing low concentrations of LA (from the preconcentrator) and ML and MeOH (from the recovery column) that add up to 0.80 m³/h. The low concentrations and volume

(relative to the makeup of cooling water needed) enable water reuse in usual water sinks such as cooling water makeup and boiler feedwater (Eslamian, 2016; Quaglia et al., 2014). In a biorefinery, potential water sinks are medium preparation for fermentation, and pretreatment such as enzymatic hydrolysis (Abdelaziz et al., 2015; Murphy et al., 1982). Hence the water consumption for the proposed process is only 0.033 m³ water/kg LA product.

3.2.5.5.5 CO₂ emissions

The CO₂ emissions are expressed as the mass of CO₂ emitted due to the combustion of natural gas for steam production (heating duty), as previously explained in section 3.2.4.3 and the equation (10), over the product mass. The base case's CO₂ emission rate (without heat integration) was 366 kg CO₂/h (for a production capacity of 3.5 ktpy of LA product), and the corresponding CO₂ emissions were 0.89 kg CO₂/kg LA product. Evidently, the introduction of indirect heat integration reduced the emissions rate to 280 kg CO₂/h, and the CO₂ emissions per unit output were reduced to 0.68 kg CO₂/kg LA.

3.2.5.6 Comparison with previous studies

The comparison between the flowsheet presented in the previous sections and the available benchmark studies was not straightforward due to additional features considered during the synthesis and conceptual design of the novel processing unit. These additional features were the reaction of the impurity (i.e., SA esterification) and higher temperature limit for the reactive zone than that of the benchmark studies (120 °C) due to using a catalyst that withstands up to 150 °C. However, the results presented and discussed hereafter provide an indication of the potential of the novel configuration using key mass and energy balance information and process performance indicators – a subset of sustainability metrics. Table 3.4 shows the key performance indicators selected to evaluate the flowsheet's behaviour, including the dual R-DWC and the benchmark studies.

Table 3.4. Process comparison in terms of key performance indicators

Parameter description		Su et al. (2013)	Kim et al. (2017)	This work
Mass balance key streams and parameters	Feed to preconcentration (kg/h)	1255.1	1255.1	1255.2
	LA to preconcentration (kg/h)	376.5	376.5	376.6
	MeOH makeup (kg/h)	6.4	6.4	26.1*
	MeOH recycled (kg/h)	311.0	310.5	406.4
	Feed to purification (kg/h)	592.4	592.8	760.5
	LA to purification (kg/h)	376.0	376.4	374.0
	Water for the hydrolysis section (kg/h)	252.2	252.2	0.0
	Impurities removed (kg/h)	67.2	67.6	73.3
	LA product (kg/h)	413.5	420.4	411.3
	Plant capacity (ktpy)	3.5	3.5	3.5
	MeOH/feed molar ratio	1.6	1.7	0.6
	MeOH/LA feed molar ratio	4.0	4.0	3.3
	LA recovery (%)	91.8	94.2	95.7
	CO ₂ emission rate (kg CO ₂ /h)	417	349	280
	CO ₂ emissions (kg CO ₂ /kg LA)	1.01	0.83	0.68
Energy used	Heating duty (kW)	1763	1474	1280
	Cooling duty (kW)	1687	1388	1177
Process performance indicators	Material intensity (kginput/kg LA)	0.379	0.357	0.256
	E-factor (kgwaste/kg LA)	0.163	0.161	0.178**
	Energy intensity (MJ/kg LA)	15.3	12.6	11.2
	Water consumption (m ³ /kg LA)	0.052	0.043	0.033
	CO ₂ emissions (kg CO ₂ /kg LA)	1.01	0.83	0.68

* Additional makeup required due to side reactions

**Higher waste production due to side reactions

The MeOH makeup flowrate found in this work was four times higher than the flowrate of the benchmark studies. This increase is attributed to the esterification of SA that consumes MeOH to produce MMS and DMS, where the latter are removed with the impurities stream, so MeOH cannot be recovered. This finding provides additional arguments in favour of the hypothesis posed that reactive impurities impact the separation of lactic acid, which has been overseen in previous studies. The additional MeOH (0.05 kg MeOH/kg LA) may impact the raw materials costs and suggest a point worth to be considered even at an early design stage. Further developments beyond the conceptual design could include a formal multi-objective optimisation procedure to target an overall performance variable (e.g., energy usage, total annual cost), making use of adequate cost correlations that account for non-conventional configurations. Meanwhile, the material intensity metric showed the lowest value for the proposed flowsheet despite the increased MeOH makeup (28–32 % reduction) because of the elimination of additional water required to perform the hydrolysis reaction by using the water produced in the esterification reaction. This outcome was achieved by appropriately placing the vapour stream from the esterification section in the hydrolysis section so that the water

required for the reaction was available in the liquid phase. The E-factor presented an increase of 10–11 %, suggesting that the proposed flowsheet produced a larger amount of waste due to the production of MMS and DMS, which feature high molecular weights. Yet, this apparently inferior performance corroborates the hypothesis that accounting for reactive impurities, even at low concentrations, can give a more realistic indication of the operating costs (i.e., additional raw materials) and the environmental performance (i.e., waste produced).

The feed stream to purification contained a similar LA amount, but this study showed a higher water amount. The benchmark studies used a conventional distillation column operating at 0.1 atm to remove approximately 88 % of water, while this work used a flash drum at 1 atm and achieved 60 % removal. Although the water removal was not as good, introducing a flash vessel made it possible to recover some low-grade heat contributing to reducing the overall energy use of the proposed flowsheet (reduction of 17 % hot utility and 22 % cold utility). Regarding the energy used, the process-to-process heat integration reduced the heating duty by 27 % and 13 % compared to the benchmarks, respectively. This result is also reflected in the energy intensity metric, where the proposed flowsheet presents the best performance.

The apparent lower capacity of the proposed flowsheet (0.54 to 2.15 % reduction) is due to the lower Di-LA content, which has a higher molecular weight, in the LA product. All products comply with the Di-LA limit of 4.4 % wt., but our flowsheet achieved a higher LA recovery than the benchmark studies. This result is explained by the fact that milder temperatures in the hydrolysis section reduced oligomerisation reactions, thus avoiding Di-LA formation, which is a form of degradation of our target molecule.

The MeOH to LA feed molar ratio in this study is the lowest, even though the amount of water entering the first column is high. This result could be attributed to the catalyst that withstands higher temperatures, so less MeOH was required to quench the reactive section.

The water consumption metric for the proposed flowsheet presents a reduction of 36 % and 22 % compared to the benchmark studies. The three principal contributions for reducing the water consumption were the lower water makeup required due to the evaporation losses (lower cooling duty), the potential reuse of the outlet water streams (e.g., cooling water makeup, boiler feedwater, medium preparation for fermentation) and the elimination of the freshwater stream to the hydrolysis section.

The total CO₂ emissions associated with the conventional sequence columns presented in the work of Su et al. (2013) was 1.01 kg CO₂/kg LA, and for the flowsheet including the fully thermally coupled column in the study of Kim et al. (2017) was 0.83 kg CO₂/kg LA. The process proposed in this work, without and with heat recovery, has figures of 0.89 kg CO₂/kg LA and 0.68 kg CO₂/kg LA, respectively. Evidently, the introduction of direct heat integration in the dual R-DWC and the process-to-process indirect heat integration allowed reducing CO₂ emissions, which positively impacted the ecological footprint.

3.2.6 Conclusions

The new methodology proposed here for the synthesis and conceptual design of a dual R-DWC was successfully demonstrated and used in an industrially relevant case study about the downstream processing of bio-produced lactic acid. The methodology followed a rule-based approach and included a combination of a decomposition method, shortcut models and rigorous simulations to obtain a robust flowsheet in which the heat recovery opportunities were fully explored and exploited. The decomposition procedure allowed the identification of the fundamental tasks that must be performed in the process, while the process synthesis and conceptual design combined these tasks effectively to generate a further intensified unit, namely a dual R-DWC that features both the forward and reverse reactions and the separation in one vessel.

Further development of the methodology is ongoing to derive a systematic approach to expand the range of processing options beyond R-DWC to synthesise advanced reactive distillation technologies. Although further case studies are yet to be carried out, the proposed approach could be evaluated in biorefinery applications for the purification of organic acids via esterification (e.g., citric acid, succinic acid, propionic acid) and the production of esters via hydrolysis or transesterification (e.g., methyl acetate, ethyl acetate, fatty alkyl esters).

Even at an early design stage, accounting for realistic and challenging characteristics (e.g., highly dilute feeds, reactive impurities) revealed the possible implications for the economics and technical feasibility when evaluating detailed designs and optimising in terms of energy usage, total annual cost, capital cost or operating cost. For example, the presence of reactive impurities in the mixture to be purified must be accounted for, as more byproducts are formed, and more raw materials are used (compared to less realistic studies based on simplified assumptions), which makes the downstream processing more complex.

The novel dual R-DWC was evaluated using process performance indicators, including relevant sustainability metrics for the conceptual design stage, which also allowed a fair comparison against benchmark processes reported in the literature. The results show that the novel dual R-DWC process proposed in this study improves sustainability, as reflected by key metrics: energy intensity of 11.2 MJ/kg LA (savings of 11–27 % vs benchmarks), material intensity of 0.256 kg_{input}/kg LA (28–32 % reduction), water consumption of 0.033 m³/kg LA (reduction of 22–36 %), and CO₂ emissions of 0.68 kg CO₂/kg LA (reduction of 18–33 %).

Abbreviations

LA	Lactic acid
SA	Succinic acid
MeOH	Methanol
ML	Methyl lactate
MMS	Monomethyl succinate
DMS	Dimethyl succinate
Di-LA	Dilactic acid
Tri-LA	Trilactic acid
PI	Process intensification
RD	Reactive distillation
R-DWC	Reactive dividing wall column
R-HiGee	Reactive high-gravity distillation
CCD	Catalytic cyclic distillation
R-HIDiC	Reactive heat-integrated distillation column
MA-RD	Membrane-assisted reactive distillation
VLE	Vapour-liquid equilibrium
UNIQUAC-HOC	Universal Quasichemical model with Hayden-O'Connell correction
NRTL-HOC	Non-Random Two liquid model with Hayden-O'Connell correction
RSA	Reactive separating agent
MSA	Mass separating agent
ESA	Energy separating agent
TAC	Total annualised cost
B/F	Bottom-to-feed molar ratio
RR	Reflux ratio
LS	Liquid split ratio

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3.3 Supplementary Information for Publication 1

The Supplementary Information presents a comprehensive reference for the calculations and setup parameters used to implement a dual-reactive dividing wall column in Aspen Plus and the corresponding results.

3.3.1 Phase equilibrium data

3.3.1.1 Validation of the thermodynamic model

The first validation was performed over the MeOH-ML pair with the experimental data from Sanz et al. (2002), which offered molar liquid and vapour fractions at 33.33, 66.66, and 101.33 kPa. Figure S3.11 depicts the experimental data points and the prediction obtained from Aspen Plus, and there is a good fit.

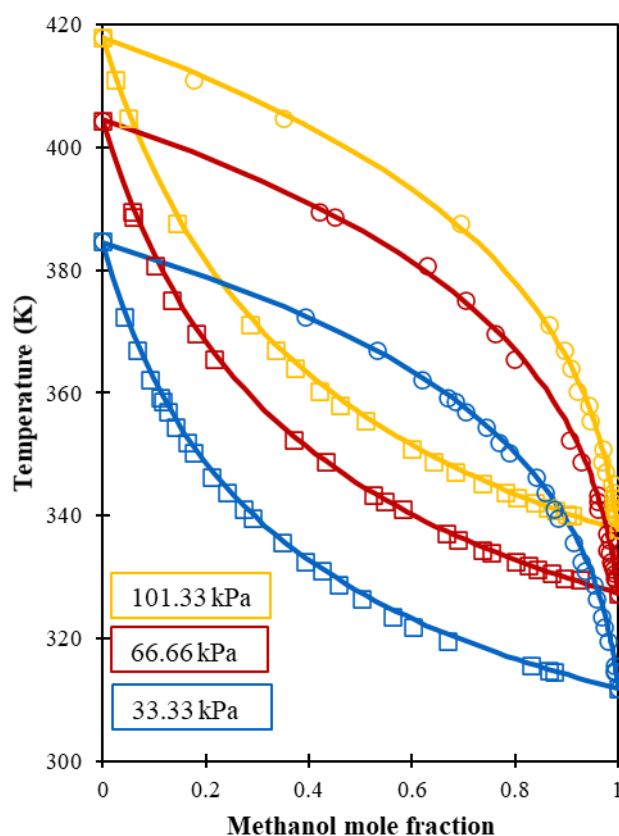


Figure S3.11. VLE validation for the methyl lactate-methanol system at different pressures (solid line: predicted values, \square : experimental mole fraction in the liquid phase, \circ : experimental mole fraction in the vapour phase)

In contrast to the SA-MeOH system, the SA-EtOH system has been widely studied, and more kinetic and VLE data are available (Altuntepe et al., 2017; Orjuela et al., 2011b). Therefore, VLE data about water-MES was used to validate the water-MMS' predicted values, where the differences in behaviour are expected to be non-significant. The work of Orjuela et al. (2011b) provided the VLE data for the water-MES system at 323.15 K. Figure S3.12 presents the

experimental data points and the predictions from Aspen Plus, and there is a good fit. As a result, the estimated binary parameters were used to build the simulation.

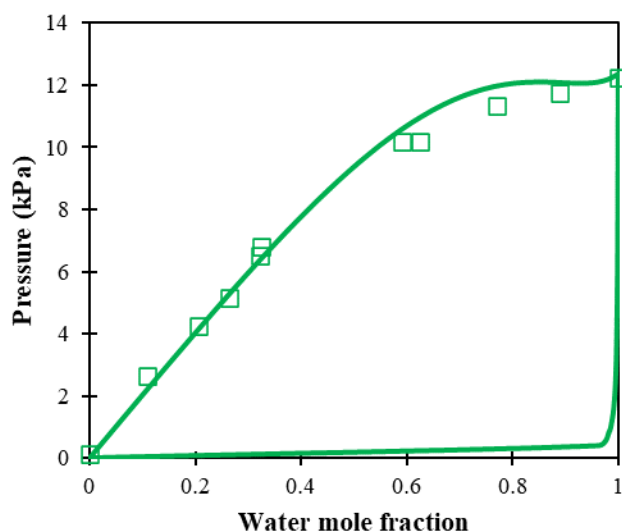


Figure S3.12. VLE validation for the monomethyl succinate-water system at 323.15 K (solid line: predicted values, \square : experimental mole fraction of water in the liquid phase)

3.3.2 Research approach

3.3.2.1 Detailed description of the decomposition approach applied to a dual reactive system

The decomposition approach, now applied to a system that includes two reactions, requires several iterations to find an adequate configuration. Once the required tasks have been identified, the inlet, outlet and internal flows needed to be located to achieve the removal, enrichment or transformation required. Thus, the preconcentrated LA and the MeOH stream were fed to the esterification column at the top and bottom of the reactive zone, respectively. The ML-rich vapour stream moved upwards to the rectifying section 1 together with the lighter products. The rectifying section 1 is expected to be small, as the main objective of the liquid stream returning to the esterification section is to maintain the downward flow of liquid, so a sharp separation is not required. The stripping section 1, below the esterification section, is meant to remove DMS and heavier components.

The vapour stream leaving the rectifying section 1 contained ML, the water necessary for the hydrolysis reaction, and the excess MeOH to be recovered and recycled. Thus, this stream was initially directed to the rectifying section 2, where MeOH and the excess water will flow upwards while ML and water were directed to the hydrolysis section to react. Then, the vapour stream leaving the hydrolysis section, rich in the light products of the reaction (MeOH), was

directed to the rectifying section 2 to remove the lightest component and the unreacted and excess water from the system.

The liquid stream leaving the rectifying section 2 is split into two streams, one returning to the rectifying section 1 and the other to the hydrolysis section, defined by the liquid split ratio. The liquid stream leaving the hydrolysis section entered the stripping section 2 to guarantee the product's specification by maintaining the ML inside the reactive zone.

The decomposition approach for the design of a DWC (Triantafyllou and Smith, 1992) and the extension for the design of an R-DWC with the reactive section in the feed side of the wall (Mueller et al., 2007) used the vapour-liquid equilibrium data to obtain the composition of the returning stream to the column on the feed side of the wall, using either a total or partial condenser. However, the configuration proposed in this work contained two reactive sections, one at each side of the wall. Therefore, the composition of the returning stream would depend not only on the separation accomplished due to the vapour-liquid equilibrium but also on the rate of consumption and production of components on the second reactive section, which is further explored when coupling both sections.

3.3.2.2 Detailed description of the shortcut calculations

Once the tasks and interconnections were placed, different system boundaries were defined to carry out mass balances. The outer system boundary contained all sections to target the top stream's compositions containing MeOH and water and the concentrated LA product stream on specification. For the inner boundary 1, full conversion of LA and SA with a stoichiometric feed of MeOH was assumed to start the calculations to update the impurities stream's flowrate and composition, which was assumed to contain only DMS. The returning stream was initially set to zero as iterative calculations are required that depend on the split ratio of the liquid stream leaving the rectifying section 2. Then, the vapour stream's flowrate and composition, leaving the inner boundary 1, were defined and used for the next calculation.

For the inner boundary 2, two streams are known, the product stream and the vapour inlet stream; while the others required initialisation, the vapour and liquid streams leaving and entering the hydrolysis section. The liquid stream entering the hydrolysis section depends on the liquid split ratio above the wall, defined as the molar flowrate returning to the esterification section over molar flowrate towards the hydrolysis section. As the objective is to drive LA production in the hydrolysis section, most ML needs to be driven to this section,

whereas avoiding drying out the upper trays in the rectifying section 1. Therefore, a liquid split ratio of 0.1 to 0.5 towards the esterification section was systematically tested by varying it with steps of 0.1. The bottom-to-feed molar ratio in the inner boundary 1 was calculated and updated accordingly. The new values for the stream leaving the esterification section were used to update the balance in the inner boundary 2.

3.3.2.3 Detailed description of the rigorous simulation of a dual-reactive dividing wall column and the recovery column at a flowsheet level

The esterification section, rectifying section 1 and stripping section 1 were implemented in a RadFrac module. The initial setup parameters included a reboiler, a total condenser and a relatively large number of stages for each section (e.g., 30). The operating pressure was selected after evaluating the boiling points and the required split, and the pressure drop was neglected at this stage of the design. The five equilibrium reactions were implemented using the built-in power law model, setting the type of reaction as kinetic and defining a liquid reacting phase. The holdup in the reactive zone was specified as the mass of catalyst, as required by the kinetic equation. A mass holdup of 10 kg per stage, used by Su et al. (2013), was employed to initialise the simulation. Structured packing was selected because of the operating pressure (mild vacuum) and the low liquid rates, in addition to the advantages of packing over trays for small columns to reduce the pressure drop and improve the separation efficiency (Pilling and Holden, 2009). The packing selected was MellapakPlus 252Y, due to its high capacity, with an HETP of 0.4 m. At the moment, Aspen Plus does not provide options for structured packing tailored for reactive distillation, such as Katapak-SP, which consists of a flexible design combining catalyst elements and MellapakPlus layers (i.e., solid catalyst included in packing) (Sulzer Chemtech, 2013). However, the similarity in the hydraulic behaviour is expected to provide an accurate estimation of the column diameter, determined with the packing sizing tool in Aspen Plus. The F-factors for the esterification and hydrolysis sections of the column range between 1.37–2.44 $\text{Pa}^{0.5}$ and 1.34–3.19 $\text{Pa}^{0.5}$, respectively. According to the data from the vendor (Sulzer), these values correspond to pressure drops of 0.4–1.5 mbar/m and 0.4–2 mbar/m, which is practically negligible. Therefore, assuming no pressure drop across the column for the simulation does not present significant changes to the material and energy balances. However, care should be taken when using internals that have a higher pressure drop per stage, as the impact could be more significant. The number of stages in each section required fine-tuning to guarantee that enough reactive stages and

catalyst holdup are available to achieve a high conversion ($> 99\%$) and that the desired separation is achieved (Al-Arfaj and Luyben, 2000). The bottom-to-feed molar ratio and the reflux ratio obtained from the shortcut calculations were used to setup the operating parameters.

The preconcentrated LA stream was initially fed in the first reactive stage, and the MeOH stream was located in the last reactive stage. As MeOH will be recovered and recycled, a mixing point was included to consider the recycling stream and the makeup. The stream representing the recycle was initialised with a MeOH flowrate in a stoichiometric ratio. The makeup stream is initialised with a low flowrate, for example, 0.01 kmol/h and adjusted after the sensitivity analysis. The logic behind selecting the MeOH flowrate (and not the MeOH-to-feed ratio) to maintain the reactive zone's temperature was based on the control loops usually used for reactive distillation and by taking into account inaccuracies of flow measurements and changes in composition (Luyben, 2013). The MeOH flowrate resulted from a design specification to maintain the last reactive stage temperature at $145\pm 2\text{ }^{\circ}\text{C}$ while varying the MeOH makeup stream flowrate. As the implementation of a thermally coupled arrangement required removing the condenser and placing a returning liquid stream, the makeup stream required adjustment. The composition and flowrate of the returning liquid stream required iterative calculations because of the separation and reaction's simultaneous occurrence. The liquid split ratio was defined in a sensitivity analysis. Convergence issues appeared during the simulation, so the operating parameters were relaxed around the initialisation values obtained from the shortcut calculations.

The hydrolysis section, rectifying section 2 and stripping section 2 were implemented in a RadFrac module, which was initially not coupled to the previous column. The initial setup included a reboiler, a total condenser and a large number of stages per section following the procedure described for the esterification column. The operating parameters defined were the bottom rate and the reflux ratio, using the shortcut calculations' results. The reactions were setup in the same manner as the esterification column. The catalyst holdup was initialised with 10 kg per stage. The inlet vapour stream was specified using the simulation's values from the previous column's top outlet stream. The flowrate of the liquid side draw was specified based on the 0.2 liquid split ratio, obtained from the sensitivity analysis. The inlet stream was initially located in the top reactive stage. The liquid side draw was located on the

stage above, so that the composition is not much varied preparing the model for the thermal coupling (Smith, 2016).

The number of stages in each section, the catalyst holdup and the inlet stage were systematically varied to guarantee a high ML conversion and avoid losing ML in the top and bottom streams. That is, the number of reactive stages was increased in steps of two, and the catalyst holdup was increased by two kilograms per stage so that the conversion and the flowrate of ML improve. In the same manner, the location of the inlet stream and the side draw were varied to minimise the loss of ML from both ends of the column. The operating parameters were relaxed around the initialisation values as the separations obtained were not sharp, and the conversion was not total. Also, the boilup ratio was set as the operating parameter instead of the reflux ratio, as the former presented a larger influence over the bottom stream. These changes were monitored with the column profiles for temperature, the liquid phase composition in each stage and the production rates, and the results of the mass and energy balances. A sensitivity analysis of the operating parameters allowed finding a combination to reach the product's target specifications while reducing the ML loss.

The coupling of both columns required several iterations that used the simulation results and updated values from the mass balances that account for non-sharp separations. Figure S3.13 describes the steps used to build the simulation in Aspen Plus. Specifically, the returning stream's composition was updated in the esterification column, which initially did not consider ML, as full conversion was assumed. Several iterations were performed by updating the vapour stream exiting the esterification column, and the liquid side stream returning to the esterification column. Once the values did not change significantly, the esterification column's vapour stream replaced the hydrolysis column's temporary stream. Additional updating was performed until the returning stream's parameters did not change, so the connection was completed. The reconciliation feature for streams in Aspen Plus and estimates of temperature, flowrate and composition for the RadFrac modules were activated to facilitate the simulation's convergence. In this manner, a previously converged simulation's initial values are in place for a new run after a significant modification is performed. More powerful convergence methods may also be needed and tested if convergence issues appear.

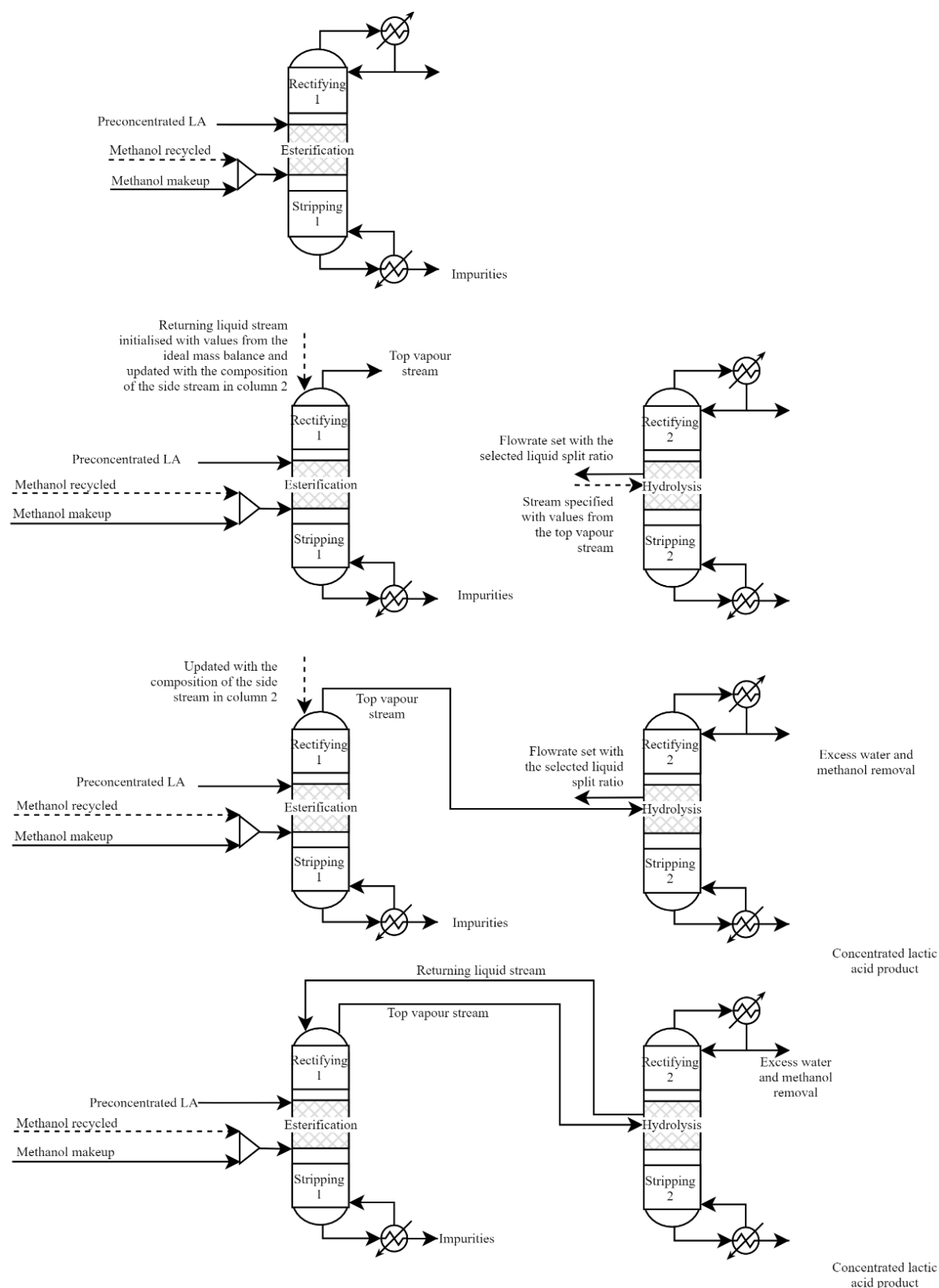


Figure S3.13. Coupling procedure for the simulation of the dual R-DWC in Aspen Plus

From the esterification-hydrolysis arrangement simulation, the distillate stream's flowrate and composition were used in the shortcut model DSW to obtain initial parameters to setup a rigorous model of the MeOH recovery column. The column was specified with a reflux ratio of one. The recovery of the light key component, MeOH, was set to a value close to one. A

total condenser and operation at one atmosphere with no pressure drop along the column were initially set. A brief sensitivity analysis was performed to vary the reflux ratio and obtain the corresponding number of theoretical stages. The purity of the MeOH stream was specified as 99 % mol. The parameters of reflux ratio, number of stages, feed stage and distillate-to-feed ratio obtained from the shortcut model were used to implement the rigorous distillation column in a RadFrac module. By varying the reflux ratio, a design specification was set to achieve a composition of the distillate stream as 99 % mol MeOH and 1 % mol water, which will then be recycled to the esterification section.

The value of the recycle stream's flowrate was updated in the temporary stream located in the mixer prior to the MeOH inlet to the esterification-hydrolysis unit, and the makeup value was adjusted manually to obtain a total MeOH feed equal to the previous converged simulation. Even though the makeup stream was adjusted with the design specification, setting an initial value closer to the “optima” value facilitated convergence. The adjustment was repeated until there was no change in the flowrate and composition of the recycle stream. The reconcile feature for streams was applied to the distillate stream from the recovery column, which was also declared as a tear stream. Finally, the recycle stream was connected, and the simulation was satisfactorily run and converged. These results demonstrated the model's robustness to operate with changing conditions and provided the mass and energy balances for evaluating the performance.

3.3.2.4 Heat integration

The stream data used for the heat integration is presented in Table S3.5. Table S3.6 presents the setup parameters for the utilities used in this study.

Table S3.5. Stream data for energy targeting

Stream number	Stream name	Supply temperature (°C)	Target temperature (°C)	Duty (kW)	Stream type
1	Feed heating	35	126	406	Cold
2	Reboiler esterification	182	183	427	Cold
3	Condenser hydrolysis	59	58	-889	Hot
4	Reboiler hydrolysis	106	107	448	Cold
5	Condenser recovery	66	65	-246	Hot
6	Reboiler recovery	98	99	267	Cold
7	Vapour from flash	105	100	-311	Hot

Table S3.6. Utilities included in the energy targeting analysis (Turton, 2018)

Utility	Supply temperature (°C)	Target temperature (°C)	Cost (\$/kW h)
Cooling water	25	30	0.0013608
LP steam	160	159	0.016344
HP steam	250	249	0.020376

3.3.3 Results and discussion

3.3.3.1 Boiling point temperatures of pure components and azeotropes at different pressures

Table S3.7 presents an extended dataset of the boiling points of the pure compounds and the azeotropes in the system at different pressures, as part of the analysis to select the operating temperature.

Table S3.7. Boiling temperatures of pure components and azeotropes at different pressures (the bold line represents the temperature limit set by the catalyst)

Component/ Azeotrope	Boiling points at different pressures							
	0.1 atm	0.2 atm	0.3 atm	0.4 atm	0.5 atm	0.6 atm	0.7 atm	
MeOH	15.67	28.60	36.80	42.95	47.91	52.10	55.74	64.53
Water-DMS	45.65	59.77	68.72	75.41	80.82	85.37	89.33	98.89
ML-Water	46.01	60.22	69.22	75.96	81.40	85.99	89.98	99.62
Water	46.06	60.35	69.41	76.19	81.67	86.29	90.31	100.02
ML	81.92	98.35	108.85	116.75	123.16	128.59	133.32	144.81
LA-DMS	125.14	143.11	154.5	163	169.86	175.64	180.66	192.75
(Di-LA)-DMS	124.89	142.91	154.41	189.3	170.06	175.98	181.13	193.61
DMS-MMS	–	–	–	–	–	–	–	–
DMS	125.24	143.61	155.43	164.36	171.63	177.81	183.21	196.37
Di-LA	150.64	167.88	178.83	187.03	193.65	199.25	204.11	215.88
LA-MMS	154.59	171.12	181.53	189.3	195.54	200.78	205.33	216.35
LA	156.52	172.46	182.56	190.12	196.22	201.36	205.84	216.63
MMS	165.14	173.66	184.83	193.21	200	205.75	210.75	222.88
SA	244.53	263.67	275.87	285.04	292.47	298.77	304.26	317.6
Tri-LA	272.25	291.8	304.2	313.46	320.94	327.24	332.71	345.9
Num. azeo.	5	5	5	5	5	5	5	6

3.3.3.2 Initialisation values for the rigorous simulation

Figure S3.14 presents a block diagram with the inlet, outlet and interconnecting streams, and Table S3.8 details the mass balance results obtained when defining a liquid split ratio of 0.4.

Table S3.8. Initialisation values from the shortcut calculations for a liquid split ratio of 0.4

Mole flowrate (kmol/h)	LA solution	MeOH feed	Impurities	Vapour to hydrolysis	Returning stream	Liquid to hydrolysis	Vapour from hydrolysis	Excess MeOH and water	Concentrated LA
MeOH	–	5.202	–	–	–	–	4.140	4.140	–
Water	14.598	0.053	–	24.495	4.642	6.963	–	12.889	–
ML	–	–	–	6.900	2.760	4.140	–	–	–
DMS	–	–	0.531	–	–	–	–	–	–
LA	4.140	–	–	–	–	–	–	–	4.140
SA	0.531	–	–	–	–	–	–	–	–

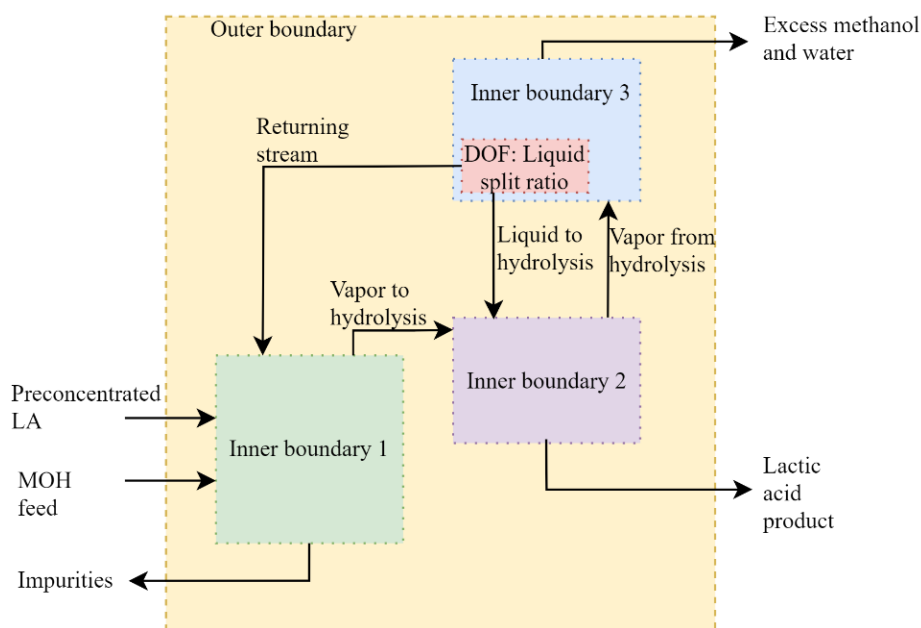


Figure S3.14. Block diagram used for the shortcut calculations

3.3.3.3 Setup parameters and results for the sensitivity analysis over the liquid split ratio

Table S3.9 indicates the setup parameters and the sensitivity analysis results where the liquid split ratio was changed from 0.1 to 0.5 in steps of 0.1.

Table S3.9. Setup parameters and results of the sensitivity analysis over the liquid split ratio

Test	Units	Test 1	Test 2	Test 3	Test 4	Test 5
Setup parameters						
Vary variable		0.1	0.2	0.3	0.4	0.5
Liquid split ratio						
Pressure	atm	0.5	0.5	0.5	0.5	0.5
B/F		0.021	0.019	0.018	0.017	0.015
Type of condenser		none	none	none	none	none
Mass holdup per stage	kg	10	10	10	10	10
Temperature constraint for reactive zone (stage 24)	°C	145	145	145	145	145
Total stages		29	29	29	29	29
Rectifying stages		4 (1–4)	4 (1–4)	4 (1–4)	4 (1–4)	4 (1–4)
Reactive stages		20 (5–24)	20 (5–24)	20 (5–24)	20 (5–24)	20 (5–24)
Stripping stages		5 (25–29)	5 (25–29)	5 (25–29)	5 (25–29)	5 (25–29)
Feed stage for LA		3	3	3	3	3
Feed stage for MeOH		24	24	24	24	24
Returning stream flowrate	kmol/h	1.23	2.78	4.76	7.40	11.10
ML	mol fr	0.37	0.37	0.37	0.37	0.37
Water	mol fr	0.63	0.63	0.63	0.63	0.63
Temperature returning stream	°C	84	84	84	84	84
Key results tracked						
MeOH feed flowrate						
makeup with a design spec in the last reactive stage	kmol/h	3.57	6.07	4.432	4.72	5.16
B/F recalculated after MeOH makeup adjustment		0.018	0.016	0.017	0.017	0.017
Top temperature	°C	87.1	86.6	88.4	89.4	90.5
Bottom temperature	°C	180.3	176.6	182.3	185.4	187.9
Reboiler duty	kW	311.1	354.5	357.9	389.1	433.2
LA conversion	%	99.54	99.96	99.40	98.94	98.99
Di-LA&Tri-LA bottom	mol fr	0.075	0.031	0.055	0.050	0.039
Impurities bottom	mol fr	0.893	0.966	0.903	0.877	0.890

3.3.3.4 Mass balance and performance indicators

Figure S3.15 presents the process flow diagram for the preconcentration and purification of LA. First, the dilute LA feed entered a flash vessel (V-1) arrangement, including a heater and a valve. The water-rich vapour stream left the system, while the liquid stream LA entered the esterification column (C-1). The impurities were removed in the bottom stream of C-1. The ML-rich stream was then fed to the reactive section in the hydrolysis column (C-2) while a liquid side-draw entered the top of C-1. The LA product was removed from the bottom of C-2. The distillate stream from C-2 entered a distillation column (C-3) to remove excess water and recover MeOH. Table S3.10 presents the flow summary for the flowsheet, and Table S3.11 presents the design features of the main vessels found to achieve the desired product.

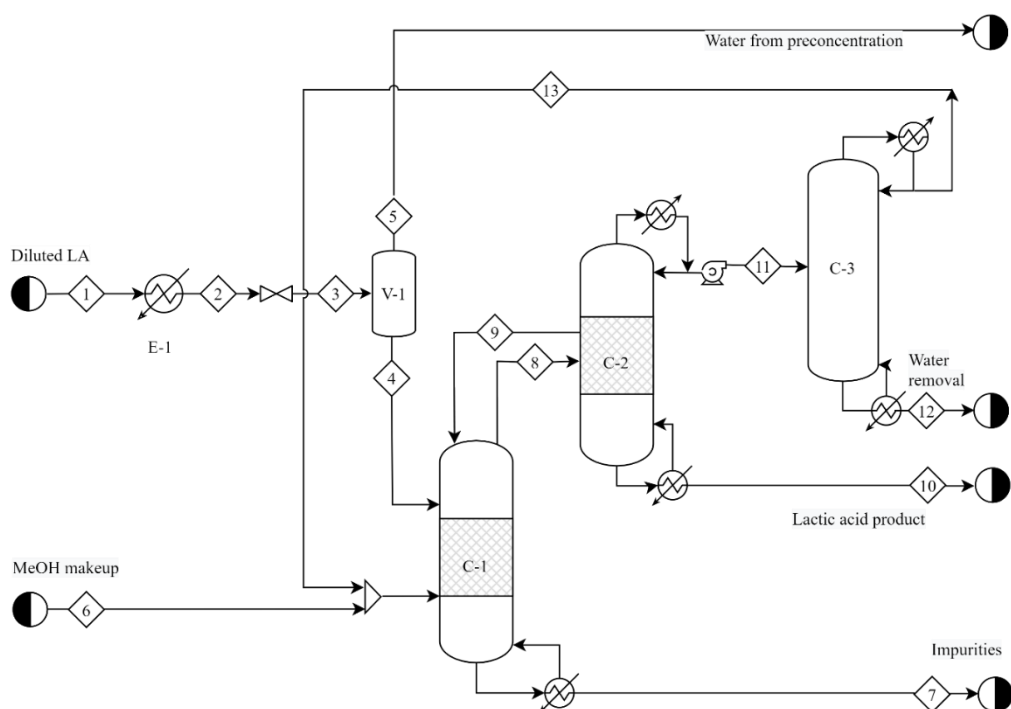


Figure S3.15. Process flowsheet developed for the preconcentration and purification of lactic acid

Table S3.10. Flowsheet stream table

Stream number	1	2	3	4	5	6
Temperature (°C)	35.0	126.0	105.4	105.4	105.4	30.0
Pressure (atm)	2.0	2.0	1.0	1.0	1.0	2.0
Vapour fraction	0.00	0.51	0.55	0.00	1.00	0.00
Mass flow (kg/h)	1255.2	1255.2	1255.2	760.5	494.7	26.1
Mole flow (kmol/h)	50.00	50.00	50.00	22.65	27.35	0.81
Component mole flowrates (kmol/h)						
Lactic acid	4.181	4.181	4.181	4.152	0.029	0.000
Dilactic acid	0.000	0.000	0.000	0.000	0.000	0.000
Trilactic acid	0.000	0.000	0.000	0.000	0.000	0.000
Methyl lactate	0.000	0.000	0.000	0.000	0.000	0.000
Methanol	0.000	0.000	0.000	0.000	0.000	0.813
Water	45.288	45.288	45.288	17.971	27.317	0.000
Succinic acid	0.531	0.531	0.531	0.531	0.000	0.000
DMS	0.000	0.000	0.000	0.000	0.000	0.000
MMS	0.000	0.000	0.000	0.000	0.000	0.000
Component mole fraction						
Lactic acid	0.084	0.084	0.084	0.183	0.001	0.000
Dilactic acid	0.000	0.000	0.000	0.000	0.000	0.000
Trilactic acid	0.000	0.000	0.000	0.000	0.000	0.000
Methyl lactate	0.000	0.000	0.000	0.000	0.000	0.000
Methanol	0.000	0.000	0.000	0.000	0.000	1.000
Water	0.906	0.906	0.906	0.793	0.999	0.000
Succinic acid	0.011	0.011	0.011	0.023	0.000	0.000
DMS	0.000	0.000	0.000	0.000	0.000	0.000
MMS	0.000	0.000	0.000	0.000	0.000	0.000

Table S3.10. Flowsheet stream table (continued)

Stream number	7	8	9	10	11	12	13
Temperature (°C)	183.1	83.0	78.2	106.9	57.6	99.2	64.7
Pressure (atm)	0.5	0.5	0.5	0.5	1.0	1.0	1.0
Vapour fraction	0.00	1.00	0.00	0.00	0.00	0.00	0.00
Mass flow (kg/h)	73.3	1200.9	79.0	411.3	710.6	301.9	408.7
Mole flow (kmol/h)	0.54	38.51	2.78	6.62	29.12	16.30	12.81
Component mole flowrates (kmol/h)							
Lactic acid	0.005	0.001	0.080	4.001	0.000	0.000	0.000
Dilactic acid	0.008	0.000	0.000	0.009	0.000	0.000	0.000
Trilactic acid	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Methyl lactate	0.000	4.459	0.250	0.028	0.082	0.082	0.000
Methanol	0.000	8.778	0.119	0.000	12.758	0.075	12.683
Water	0.000	25.276	2.332	2.579	16.275	16.147	0.128
Succinic acid	0.128	0.000	0.000	0.000	0.000	0.000	0.000
DMS	0.224	0.000	0.000	0.000	0.000	0.000	0.000
MMS	0.179	0.000	0.000	0.000	0.000	0.000	0.000
Component mole fraction							
Lactic acid	0.009	0.000	0.029	0.605	0.000	0.000	0.000
Dilactic acid	0.016	0.000	0.000	0.001	0.000	0.000	0.000
Trilactic acid	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Methyl lactate	0.000	0.116	0.090	0.004	0.003	0.005	0.000
Methanol	0.000	0.228	0.043	0.000	0.438	0.005	0.990
Water	0.000	0.656	0.839	0.390	0.559	0.990	0.010
Succinic acid	0.234	0.000	0.000	0.000	0.000	0.000	0.000
DMS	0.412	0.000	0.000	0.000	0.000	0.000	0.000
MMS	0.330	0.000	0.000	0.000	0.000	0.000	0.000

Table S3.11. Flowsheet design results

Parameter	C-1	C-2	C-3
Pressure (atm)	0.5	0.5	1
Total number of trays	25	85	30
Number of rectifying stages	8	10	15
Number of reactive stages	12	30	–
Number of stripping stages	5	45	15
Catalyst mass per stage (kg)	10.0	12.0 (11–40) 14.0 (41–80)	–
Maximum stage liquid holdup (m ³)	0.00478*	0.00262*	0.00129
Feed stage	6 (LA) 20 (MeOH)	21	16
Condenser duty (kW)	0	889	246
Reboiler duty (kW)	427	448	267
Diameter (m)	0.67	0.57	0.33

* The liquid stage holdup corresponds to 3 % of the total stage volume with a HETP of 0.4 m, assuming a catalyst occupancy of 50 % of the holdup volume and a catalyst bulk density of 800 kg/m³

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3.4 Perspective on Publication 1

The development of a process flowsheet, presented in Publication 1, used published configurations containing a sequence of reactive distillation and conventional distillation as the benchmark. Modelling and analysing the behaviour of this sequence gave insight into intensified alternatives to hypothesise that R-DWC could provide benefits based on the already known performance of individual RD and DWC. This study raised questions about the possibility of developing a systematic approach for process synthesis and evaluation.

Identifying key basic properties and kinetic parameters, evaluated when building the conceptual design, helped formulate appropriate questions that could be extended to evaluate the potential benefits of advanced reactive distillation. These questions aimed to engender an understanding of the chemical system and its behaviour in a dual R-DWC configuration. Observed effects were primarily caused by the byproducts of side reactions, which needed to be removed. Also, the reaction caused additional azeotropes to form. These insights stimulated the development of a conceptual framework founded on high-level questions. Such a framework is proposed in Publication 2 in Chapter 4.

The conceptual design presented in Publication 1 executed several sensitivity analyses to explore the effect of varying available degrees of freedom to promote the desired separation, conversion, and product specifications. The sensitivity analyses helped identify suitable values, particularly operating conditions. This observation underpinned the development of a procedure to define operating windows appropriate to advanced reactive distillation technologies, presented in Publication 3 in Chapter 4.

The questions that arose from the conceptual design study in Publication 1 and the evaluation of additional case studies helped to identify the need for a structured methodology that enables the technical feasibility of advanced reactive distillation technologies to be assessed in the early stages of process design. Publication 4, included in Chapter 5, develops and presents the resulting methodology.

Chapter 4

Development of a conceptual framework and operating windows as a basis to aid the synthesis of advanced reactive distillation technologies

4.1 Preface to Publications 2 and 3

Chapter 4 contains Publication 2, its unpublished Appendix, and Publication 3 with its Supplementary Information. Chapter 4 addresses the following objectives of this PhD thesis:

3. To define the scope, limitations and data relevant to the synthesis of advanced reactive distillation technologies in a conceptual framework by identifying basic thermodynamic properties and kinetic parameters and by formulating high-level questions using the conceptual design of a dual R-DWC and case studies reported in the literature
4. To identify and represent potential interactions between advanced reactive distillation technologies and chemical systems by extending the concept of operating windows to identify and expand suitable operating regions and to test the proposed procedure with relevant case studies

Publication 2 proposes a conceptual framework to define the basis and scope of the methodology to be developed. The basis includes high-level questions, relevant thermodynamic and kinetic properties of pure components and mixtures, and liquid-phase reactions, including side reactions. Relevant operating constraints relate to process materials (chemical compounds, catalysts, materials of construction). Inaccuracies may arise from limitations of models for predicting the behaviour of chemical systems.

The purpose of the Appendix to Publication 2 is to provide details on the approach applied to develop the conceptual framework. This section discusses how case studies from the

literature have been used to underpin the research approach, the development of the methodology and the testing and verification of the resulting flowsheets.

The learnings from the conceptual design study presented in Chapter 3 and Publication 2 stimulated the development of a procedure to build operating windows suitable for advanced reactive distillation technologies in Publication 3. Operating windows enable the user to assess the type of chemical system to which these technologies can be applied.

Operating windows facilitate visualisation of regions where the reaction and separation can take place using a pressure vs temperature diagram. New concepts of 'representative components' and a 'sliding window' are introduced to help capture the complexity of the system while expanding the range of feasibility compared to reactive distillation only. Accounting for a fuller range of multicomponent mixtures, two 'representative components' – light and heavy – are identified by applying simplifying assumptions to provide boundaries for the operating windows. A 'sliding window', when superimposed over the pressure vs temperature diagram, moves along the temperature axis, following heuristics and first principles, to identify suitable ranges of temperatures and pressures, while providing insights for selecting advanced reactive distillation technologies. These outcomes accompany flowsheet development and help to answer some of the high-level questions used in the synthesis methodology, as detailed in Chapter 5. The application of the procedure is demonstrated and analysed in three case studies:

- Methyl acetate production
- Lactic acid concentration and purification
- Tert-amyl methyl ether production

4.2 Publication 2

Title: Synthesis of advanced reactive distillation technologies: Early-stage assessment based on thermodynamic properties and kinetics

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Synthesis of Advanced Reactive Distillation Technologies: Early-Stage Assessment Based on Thermodynamic Properties and Kinetics

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Abstract

In the early stages of process design, the design space is huge, often requiring simplified models that are based on conventional unit operations with their inherent strengths and limitations. In this paper, we present a novel conceptual framework and a synthesis methodology applied to a specific design problem featuring an equilibrium-limited reaction or a separation that can benefit from the introduction of a reactive separating agent to use intensified technologies born from the success of reactive distillation. Two case studies (related to lactic acid and dimethyl ether production) illustrate the application of the synthesis methodology, and the outcomes are verified with conceptual design studies reported in the literature.

Keywords: Process synthesis; Reactive distillation; Process intensification; Feasibility methodology; Fluid separations

4.2.1 Introduction

Chemical industries face multiple challenges due to increasing competitiveness, tighter regulations, and more stringent technical, commercial, safety and environmental requirements. The conventional process synthesis and design approaches to serve chemical industries generally apply established unit operations which are continuously challenged to reach new targets. Also, the increase in computing power has benefited the development of complex superstructure optimisation methods combining synthesis and design simultaneously and including economic and sustainability indicators. As a result, the increased complexity requires numerous assumptions to simplify the models and often neglects important characteristics of the system that can impact process design in later stages. On the other hand, understanding a chemical system is crucial in the early stages of process design, for example, during flowsheet development.

Therefore, this work focuses on a much smaller subset of the design problem and proposes a methodology for early-stage process design to quickly evaluate advanced reactive distillation technologies that incorporate additional intensification features to reactive distillation (RD). These advanced RD technologies can be applied to equilibrium-limited reactive systems in the liquid phase or fluid separations that can benefit from the introduction of a reactive separating agent (RSA) to facilitate the separation. Decision-making for process synthesis is guided by high-level questions about the chemical system of interest, which can be answered by knowing basic thermodynamic properties and kinetic data and using experience or experts' knowledge from conventional RD applications.

4.2.2 Advanced reactive distillation technologies

The technologies included in the scope of the synthesis methodology were developed following the success of RD by evaluating additional intensification features to expand the operating window and find potential new applications. The technologies considered here are reactive dividing-wall column (R-DWC), catalytic cyclic distillation (CCD), reactive internally heat-integrated distillation (R-HIDiC), reactive high-gravity distillation (R-HiGee), and membrane-assisted RD (MA-RD). Figure 4.1 illustrates the key features of the five technologies included in the scope of this study and highlights their advantages compared to RD.

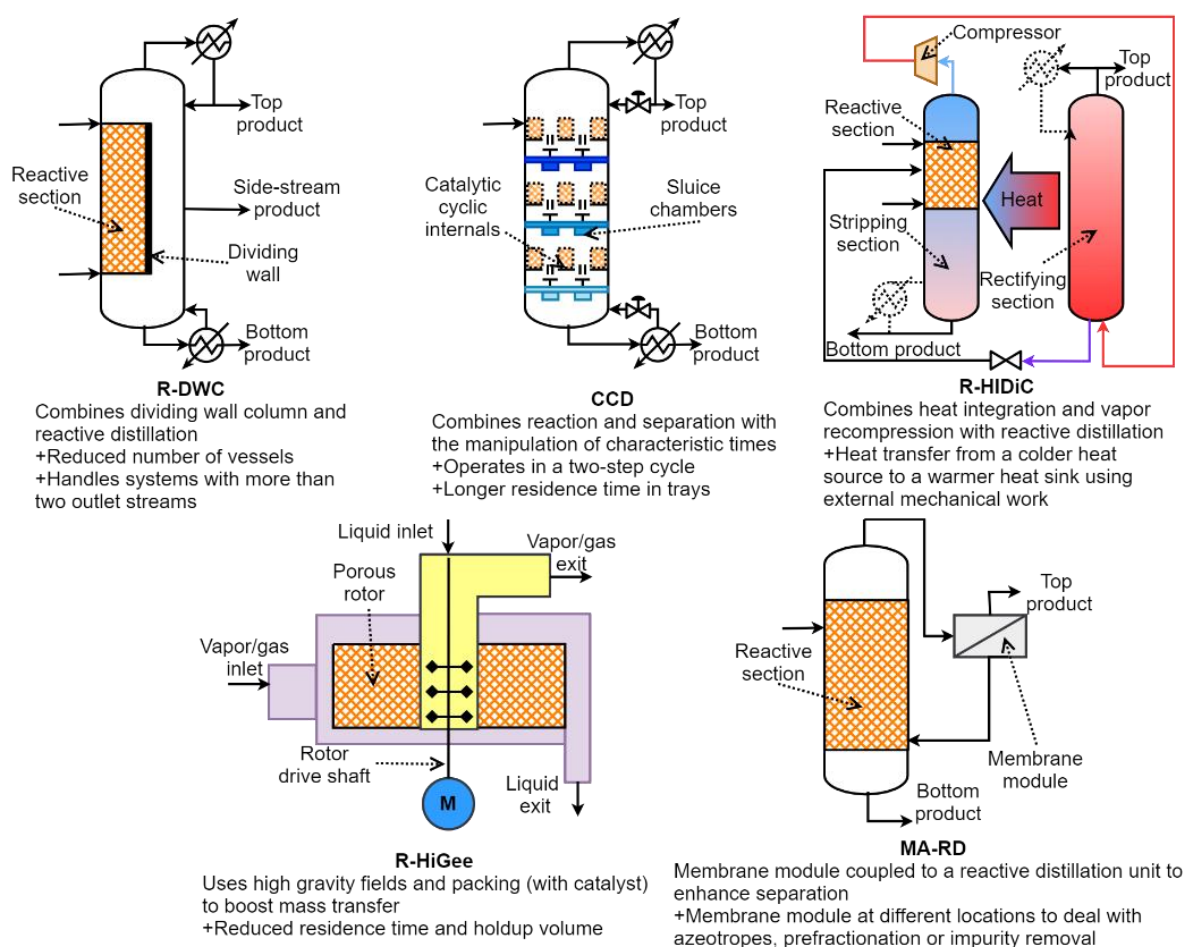


Figure 4.1. Main features of the five advanced reactive distillation technologies

4.2.3 Research approach, conceptual framework and scope

4.2.3.1 Research approach

Kiss et al. (2019) noted that advanced RD technologies had not reached maturity due to the lack of robust methods and tools for process design and simulation, process dynamics and control, lack of pilot and industrial tests, and because of practical challenges related to ease of implementation. However, the range of applications of conventional reactive distillation is well established for equilibrium-limited reaction systems that have been studied on a laboratory, pilot or industrial scale (Luyben, 2013; Skiborowski, 2018). The ongoing research and developments about advanced distillation technologies (Kiss, 2013) and the knowledge and understanding of various chemical systems – feed and product specification, kinetics, phase equilibria, catalysts and operating conditions – are the basis for the decision-making methodology that aims to include advanced RD technologies in the early stages of process design.

4.2.3.2 Conceptual framework and scope

The methodology aims to be general enough to cover a wide range of equilibrium-limited reaction systems and their characteristics relevant to large-scale industrial applications (e.g., azeotropes, impurities and trace components, difficult separations). These characteristics are often simplified in laboratory-scale investigations, such as considering pure feeds, a large amount of solvent, and not accounting for the type of utilities needed. As a result, these characteristics usually lead to the need for multiple processing steps. However, the use of intensified technologies that combine reaction and separation may overcome these challenging characteristics resulting in more compact and efficient processing units.

Figure 4.2 shows the conceptual framework of the decision-making methodology proposed in this work, which prompts high-level questions to the user to know the chemical system better. These questions can be answered given thermodynamic properties and kinetic parameters, and the most common sources of information are indicated.

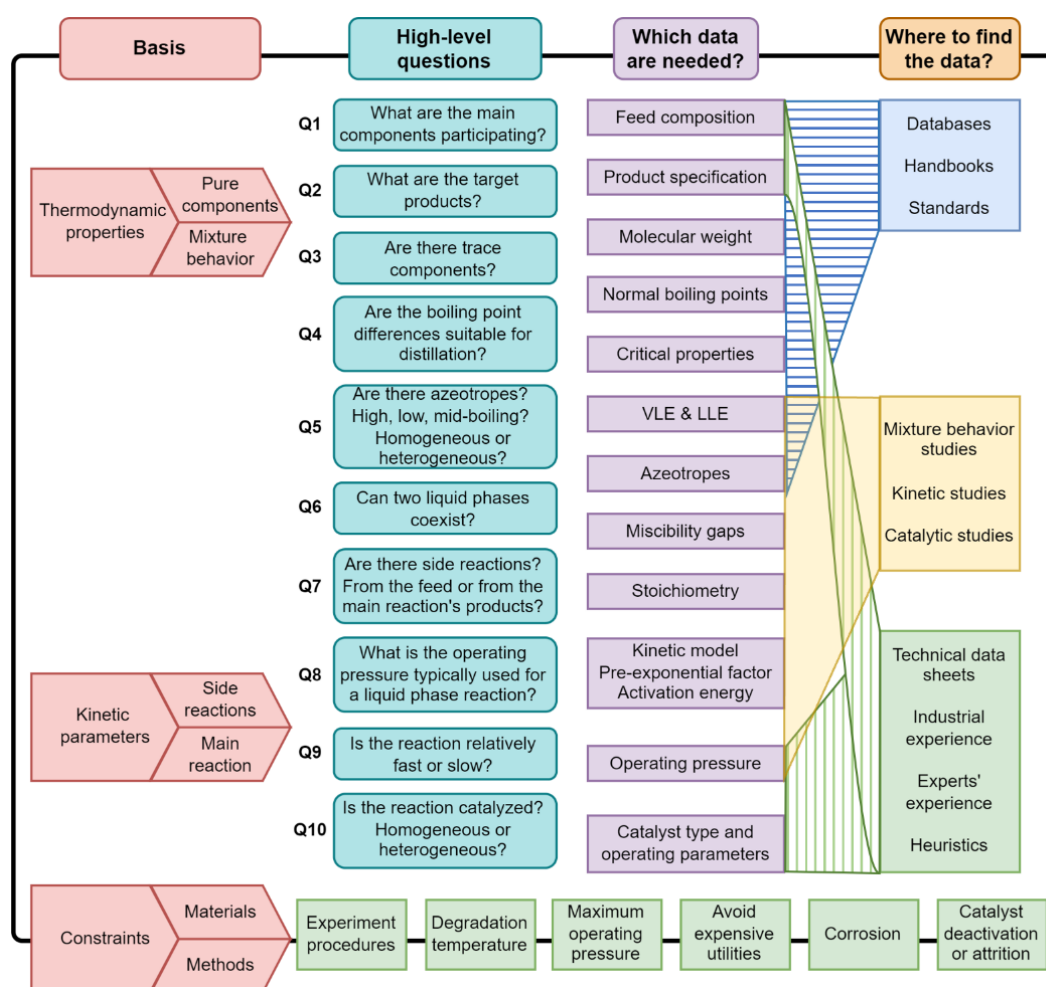


Figure 4.2. Conceptual framework for the synthesis of advanced reactive distillation technologies

Thermodynamic property data of pure compounds and mixtures include process stream compositions (feeds and products), basic physical properties and phase equilibrium information. This information can be easily gathered from databases and handbooks, experiments or robust equations of state and activity coefficient models.

The kinetic parameters of the main reaction must be carefully identified, along with relevant side reactions that are often neglected in the conceptual design. For example, a parallel reaction can compete with the main reaction (consuming a reactant), or a series reaction can consume a product. Therefore, potential side reactions and their impact must be thoroughly understood at early stages because neglecting them can drive the decision-making process towards infeasible designs that may not be able to handle or overcome such complexities.

Information about thermodynamic properties and kinetics parameters can guide selection, but decisions also need to take into account constraints imposed by materials (i.e., catalysts, materials of construction) and methods (e.g., kinetic studies validity). The materials account for the chemicals used, the catalyst (functions, robustness against deactivation, thermal and mechanical performance, availability for large-scale applications), and the materials used for vessels, column internals, membranes, and fluid handling system. The methods include laboratory procedures to evaluate kinetics or mixture behaviour and the rating and sizing associated with conditions inherent to the system, such as operating pressure and temperature, moving parts, corrosive environment, or abrasive materials.

4.2.4 Decision-making methodology applied to two case studies

The high-level questions shown in Figure 4.2 are the backbone of the decision-making methodology. These questions firstly address the feed composition and the expected products and byproducts, considering dilution, trace components and impurities. The next set of questions refers to the operating conditions: operating pressure and the range of temperatures expected. The next step deals with the reactions identified in the system, where the forward reaction rate constant of the main reaction is evaluated at 363.15 K to categorise its rate as relatively slow, average, or fast. Side reactions are then evaluated according to the source of the reactants: from the feed stream, which can drive parallel reactions; or from the main reaction products, which can trigger a series reaction. Finally, the mixture behaviour is evaluated by understanding the phases present and the existence of azeotropes.

We illustrate the application of the decision-making methodology in two case studies. A brief introduction about each chemical system allows the high-level questions to be answered. In each case study, relevant decision points that guide the technology selection are examined along with an excerpt of the decision-making flowchart.

4.2.5 Results and discussion

4.2.5.1 Concentration and purification of lactic acid

The feed consists of a pre-treated fermentation broth that contains lactic acid (LA) (30 % wt.), succinic acid (5 % wt., reactive impurity), and a large amount of water. The design problem involves a separation to remove water and other acid impurities to obtain food-grade LA (88 % wt.). We introduced a reactive separating agent (RSA), methanol, to promote the esterification LA to produce methyl lactate and water with a heterogeneously catalysed equilibrium-limited reaction of the type $A + B \rightleftharpoons C + D$. Succinic acid also reacts to produce heavy succinates. Once the heavier succinates are removed, the reverse hydrolysis reaction is promoted by providing sufficient water in the liquid phase to obtain LA on specification and free from the impurity.

Relevant answers used in the decision-making flowchart are that the feed is dilute (Q1); the streams identified are product, byproduct, excess water, and the RSA (Q2); the operating pressure should be sub-atmospheric to avoid thermal degradation (Q8); the existence of parallel side reaction from the impurity in the feed (Q7); the existence of homogenous mid boiling azeotropes (Q5), which are presented in an excerpt of the decision-making flowchart in Figure 4.3a.

The main outcomes are that a preconcentration step is required to remove excess water. Among the advanced RD technologies evaluated, the R-DWC is deemed suitable due to the number of outlet streams required, the side reaction byproducts and the presence of mid-boiling azeotropes that can be consumed in the reactive sections. In addition, R-HiDiC and CCD are discarded because of their limitations in operating under vacuum. These outcomes were supported by conceptual design studies about thermally coupled configurations (Kim et al., 2017) and a dual R-DWC (Pazmiño-Mayorga et al., 2021), which demonstrated energy savings compared to a conventional RD.

4.2.5.2 Production of dimethyl ether (DME)

A feed of pure methanol reacts to produce water and dimethyl ether (99.5% mol). Conventional DME production requires high temperatures and pressures and several unit operations. Here, the design problem involves a heterogeneously catalysed liquid-phase reaction of the type $A \rightleftharpoons B + C$.

The main characteristics driving decisions for technology selection are illustrated in Figure 4.3b. The reaction rate constant is relatively slow in the framework of RD applications (Q9), the presence of a small two-phase liquid region (Q6) and the absence of azeotropes (Q5).

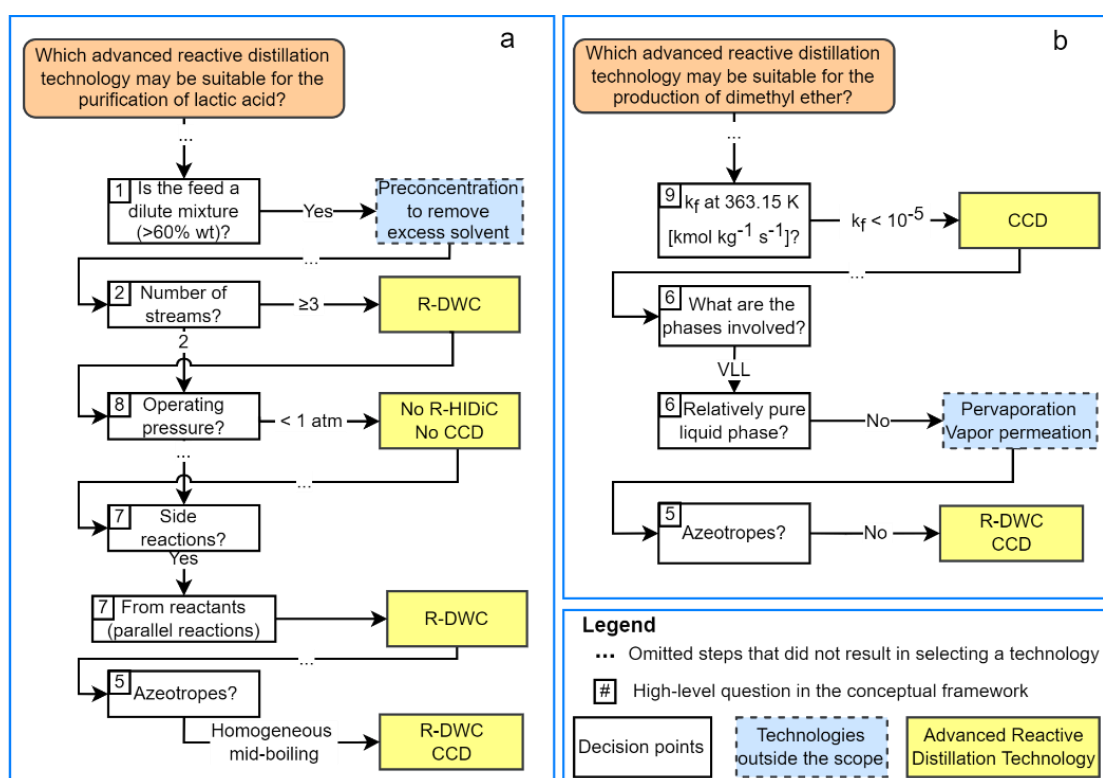


Figure 4.3. Excerpt of the decision-making methodology and outcomes a) lactic acid purification b) dimethyl ether production

The technologies deemed suitable for DME production are CCD, as larger holdups allow longer residence times suitable for the relatively slow reaction. The absence of azeotropes enables the application of R-DWC and CCD without risking the purity of the outlet streams. However, the existence of a small two-phase region suggests that auxiliary equipment may be needed to remove water, such as a membrane. These outcomes were demonstrated with the conceptual design study of an R-DWC that showed energy saving compared with conventional RD (Kiss and Suszwalak, 2012). Also, DME production in a CCD has been studied

at the conceptual level (including a patent), indicating that higher purities can be achieved with fewer stages and a lower vapour flowrate (Pătruț et al., 2014; Kiss et al., 2015).

4.2.6 Conclusions

This work showcases a decision-making methodology for the synthesis of advanced RD technologies using chemical system data that can be easily obtained at early stages during flowsheet development. The highlights are the inclusion of novel intensified technologies that are often dismissed in traditional process design settings, the use of thermodynamic properties and kinetic parameters of the chemical systems and the pool of established heuristics from recent research about RD and advanced distillation. The methodology is demonstrated in two case studies. The outcomes are verified by the results of published studies. A more detailed description of the methodology is under preparation with further case studies to evidence its range of applicability.

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4.3 Appendix to Publication 2: Research approach for developing a synthesis methodology

This appendix serves two main purposes. First, it aims to expound upon the concepts introduced in Publication 2 to provide a more comprehensive understanding of the motivation and rationale that underpinned the development of the conceptual framework and synthesis methodology presented in Publication 4. Secondly, this appendix elucidates the use of case studies as a research method, detailing how they were employed to explore the subject area, generate hypotheses, and test and verify the synthesis methodology across a range of chemical systems. Overall, this appendix aims to provide a deeper insight into the research approach used in this PhD thesis, with the intention of enhancing the reader's understanding of the research and its development.

4.3.1 Establishing a conceptual framework

In recent years, research has focused on process intensification combined with process design and optimisation, demonstrating the uptake of process systems engineering tools (i.e., superstructure optimisation) (Alcántara Avila et al., 2021). The literature review revealed that advanced reactive distillation technologies do not usually appear in the initial superstructure or technologies portfolio. Frequently, computer-aided tools are used to identify solutions, but these solutions can turn out to be infeasible (Tula et al., 2020).

Past case studies evaluating the technical feasibility of a particular advanced reactive distillation technology did not elucidate why these technologies were chosen in the first place. This research gap motivated the development of a synthesis methodology specifically tailored to these technologies, beginning with establishing a sound theoretical basis. The conceptual framework in Publication 2 formed the basis for developing the synthesis methodology while outlining its scope.

4.3.2 High-level questions

The high-level questions proposed in this conceptual framework aim to carry out an exploratory investigation, where the requirement for accurate physical properties is less than that for detailed design (Smith, 2016). High-level questions are similar to the "rules" applied in ruled-based methodologies (Gani et al., 2022; Tula et al., 2020).

In this PhD thesis, thermodynamic properties and kinetic parameters are essential to answer the proposed high-level questions. The availability of these data is crucial for process synthesis and design. Retrieving data from a range of open sources expedites the initial exploratory evaluation, partly because no proprietary information is required. The information required

to satisfy the high-level questions could be obtained from handbooks, publications, books and rules of thumb. However, preparation and validation of these data are required to obtain an accurate representation of the chemical systems. An example of the validation procedure is presented in the Supplementary Information of Publication 1, where experimental data is used to validate the thermodynamic models applied.

4.3.3 Case studies to explore the subject area and generate hypotheses

Defining the design problem is the first step for process design, where the characteristics of the feed, the product specifications and additional considerations need to be stated. Typically, laboratory-scale investigations and simulations use methods developed with simplifying assumptions that are applicable to simple models or ideal chemical systems (Seider, 2017). However, applying these methods to real chemical systems can lead to inaccurate or misleading results. Therefore, case studies accounting for real chemical systems were studied to inform the development of the methodology, which accounts for the inherent complexities of advanced reactive distillation and those of the multicomponent chemical systems by a) selecting chemical systems for which reactive distillation is applicable and b) evaluating applications of advanced reactive distillation.

a) Selecting chemical systems for which reactive distillation is applicable

A four-step procedure was used to shortlist chemical systems to aid the development of the methodology.

- Step 1: Search for previous applications in reactive distillation
- Step 2: Review potential as a finished product or a platform chemical
- Step 3: Assess whether annual production is suitable for continuous operation
- Step 4: Identify relevant characteristics of the chemical system

In Step 1, a list of real chemical systems reported by Luyben and Yu (2008) provides information about the type of reaction in terms of stoichiometry and the source where the application to reactive distillation is reported. Then, the results from a search in recent literature using keywords such as the compound's name, combined with reactive distillation or a specific advanced technology, were added to the list.

In Step 2, the role of the chemical participating in the reaction, either as a reactant or product of the reaction, was gathered from the *Kirk-Othmer Encyclopedia of Chemical Technology*,

Ullmann's Encyclopedia of Industrial Chemistry, the *Dictionary of Chemistry* from the Oxford University Press and original papers to help define the design problem.

In Step 3, relevant literature and market reports (e.g., ICIS Market price report) provided information about the global annual production of the chemical. A heuristic rule suggests that a plant with a capacity greater than 5000 t/year should operate continuously, while plants with less than 500 t/year operate batch-wise (Douglas, 1988). Continuous operation is preferred in advanced reactive distillation technologies.

Finally, step 4 identified relevant characteristics of the chemical system, particularly usual operating pressures and temperatures.

Studies about the purification of lactic acid in reactive distillation (Alves de Oliveira et al., 2018; Cho et al., 2008; Dai et al., 2019; Gao et al., 2007; Itimura et al., 2015; Kim et al., 2017; Su et al., 2013) motivated the selection of this process as the starting point to understand the complexities involved in the conceptual design of advanced reactive distillation technologies, as presented in Publication 1. The research approach used for the conceptual design study of lactic acid was adapted to be applied to any chemical system where advanced reactive distillation might offer benefits over conventional processes. In other words, the study of lactic acid served as a model for developing and testing a generalisable approach that could be used for the early-stage design of advanced reactive distillation processes for a wide range of chemicals.

b) Evaluating applications of advanced reactive distillation

In the process of investigating applications of advanced reactive distillation technologies, details of the reactants and products (hence the type of reaction), type of catalyst, operating conditions, thermodynamic and kinetic models used, methods for evaluation (experimental or simulation-based), optimisation, control and industrial applications were gathered. This information helped to identify case studies for developing the synthesis methodology, and the processes selected for learning and training are detailed in Table 4.1.

Table 4.1. Selected processes used for training

Technology	Case studies for training
R-DWC	Purification of lactic acid (Kim et al., 2017; Su et al., 2013) Dimethyl ether production (Kiss and Suszwalak, 2012) Biodiesel production (Kiss et al., 2012)
R-HiGee	Esterification of acetic acid (Krishna et al., 2012) Hydrolysis of methyl lactate (Gudena et al., 2013b) Synthesis of hypohalous acid (Quarderer et al., 2000)
R-HIDiC	Tert-amyl ether production (Babaie and Nasr Esfahany, 2020; Pulido et al., 2011)
CCD	Dimethyl ether production (Pătruț et al., 2014)
MA-RD	Purification of lactic acid (Gudena et al., 2013a)

Through evaluating the case studies, characteristics of chemical systems that make a particular advanced reactive distillation technology advantageous were identified. These findings are summarised in Table 4.2 and incorporated into the methodology to define "decision points". These decision points suggest when one technology is more beneficial than another. The flowchart and associated decisions are expanded upon in Chapter 5.

Table 4.2. Key characteristics of the chemical systems that can be exploited in advanced reactive distillation technologies

Technology	Characteristics of the chemical systems	Potential decision points
R-DWC	Boiling points	If one of the components of interest is a middle boiling component that can be obtained as a side stream
R-HiGee	Rate of reaction Series reactions	When the reaction is fast When there are undesired series reactions
R-HIDiC	Boiling points at ranges of pressures Compression ratio for an economic operation	A relatively small pressure difference is needed between rectifying and stripping sections to enable the distillate to be warmer than the bottom product
CCD	Rate of reaction Maybe for diffusion (mildly) limited systems	If the reactions are equilibrium-limited and relatively slow at the temperature and pressure of interest and require longer residence time than in conventional reactive distillation
MA-RD	Azeotropes	When a membrane can selectively remove one or more compounds, especially if the components to be separated are close-boiling or form an azeotrope

4.3.4 Case studies for testing and verification of the synthesis methodology

Case studies from the research literature were used to test and verify the synthesis methodology, as well as to identify its limitations. These studies covered various aspects, such as experiments, modelling, simulation and optimisation, which evaluated economics, sustainability assessment, degree of intensification, and computing time. Qualitative and quantitative indicators of flowsheets presented in the literature were compared to test and

verify the outcomes of the synthesis methodology. These indicators provide insight into the relative "success" that a particular application has when it is tested experimentally or in a rigorous simulation. The resulting flowsheets from the synthesis methodology were verified and classified as "successful" when the synthesis methodology also identified the advantages or disadvantages found in the case studies from the research literature.

The processes selected are:

- i. Lactic acid purification
- ii. Methyl acetate production
- iii. Dimethyl ether production
- iv. Tert-amyl methyl ether production
- v. Benzene to cyclohexane process
- vi. Isooctane production
- vii. Biodiesel production

The synthesis methodology presented in Chapter 5 was tested in processes i to v above, which had sufficient information for the application and analysis of the methodology. Limitations of the methodology were identified from processes vii and viii, also presented in Chapter 5.

4.3.5 Creating a systematic methodology for the synthesis of advanced reactive distillation technologies

At the beginning of the development of the conceptual framework, high-level questions were used randomly. After various iterations of testing high-level questions with different chemical systems identified in sections a) and b), it became evident that they needed to be systematically arranged to facilitate their application. In this way, the use of case studies from the research literature helped refine and structure the decision-making flowchart for the synthesis methodology.

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4.4 Publication 3

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Operating windows for early evaluation of the applicability of advanced reactive distillation technologies

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Highlights

- Process intensification enabled via advanced reactive distillation technologies
- Operating windows construction to expand the applicability of reactive distillation
- Simplification strategies to represent multicomponent systems in operating windows

Abstract

Advanced reactive distillation technologies (ARDT) are often overlooked during process synthesis due to their complexity. This work proposes the use of operating windows with additional features to identify suitable operating limits for ARDT. Data needed to construct the operating windows are thermodynamic properties, kinetic parameters, constraints of materials and experimental methods, and heuristics. In addition, two new concepts are proposed to represent complex features: representative components and a sliding window. Results include the identification of suitable operating limits for ARDT to help assess their feasibility early in process design. The proposed approach is demonstrated by case studies. Methyl acetate production can be carried out at low pressures (0.5–3.6 atm), while lactic acid purification requires vacuum conditions (0.3–0.8 atm) to avoid thermal degradation. Tert-amyl methyl ether production was evaluated in two scenarios where the effect of side reactions is evidenced in a reduction of the reaction window due to temperature limits to favour the main reaction over the side reaction. This study is the first to evaluate advanced reactive distillation technologies using a graphical representation in an operating window to aid process synthesis, where the results provide key selection insights.

Keywords: Process intensification; operating windows; process synthesis; reactive distillation

4.4.1 Introduction

Sustainable development is essential for the progress of chemical process industries. The search for efficient chemical processes looks beyond revenue and quality to consider environmental and social impacts (Azapagic et al., 2006). Therefore, innovation is needed in process design practice. Process Intensification (PI) can substantially improve energy and material efficiency, costs, process safety and waste reduction (Moulijn and Stankiewicz, 2017). PI theory and guidelines in design and innovation can contribute to the realisation of the Sustainable Development Goals (Harmsen and Verkerk, 2020). Reactive distillation (RD) is a successful example of PI that combines reaction and separation in a single unit. The separation is improved as the reaction overcomes azeotropes, and the reaction improves because the separation helps overcome chemical equilibrium and improves reaction rates, conversion, and selectivity due to the constant removal of the reaction products. The advantages of RD include capital and operating cost savings, smaller plant footprint, fewer recycled streams, and better environmental performance (Sundmacher and Kienle, 2003; Kiss, 2017). However, RD requires that the reaction and separation take place under similar operating conditions, represented using 'operating windows' (Luyben, 2013; Orjuela et al., 2016). Advanced reactive distillation technologies (ARDT) combine the principles of RD and additional intensification techniques that could extend the range of operating conditions and expand the applicability of RD (Kiss et al., 2019).

An operating window is a graphical representation that links material streams' properties and process units to identify feasible operation regions. Typical operating window boundaries include pressure, temperature, pH value, residence time or concentration (Schembecker and Tlatlik, 2003; Recker et al., 2015). The combination of pressure and temperature allows for evaluating equilibrium data associated with separations, reaction kinetics and the mechanical design of equipment. Operating windows are commonly used to identify potential economic trade-offs and to reduce the design space (Tylko et al., 2006; Recker et al., 2015). Limiting the number of process alternatives can inform future experimental and modelling work (Leng et al., 2012; Steimel et al., 2014) or help define design specifications for evolutionary search optimisation (Steimel et al., 2013). Regarding existing processes, operating windows allow to evaluate the flexibility of boundary conditions to meet production targets safely (Leng et al., 2012; Riese and Grünewald, 2020). For combined reaction-separation operations, operating windows have been used to evaluate the feasibility of RD (Orjuela et al., 2016; Kiss, 2019).

Operating windows are built using basic information typically accessible in the literature (Tylko et al., 2006), such as experimental data, shortcut or rigorous models (Steimel et al., 2014). Holtbruegge et al. (2014a) and Kraume et al. (2022) agree that experts' experience is fundamental to establish operating windows, particularly regarding pressure limits. Although engineers' knowledge can significantly reduce the effort of gathering information to support decision-making, Steimel et al. (2014) showed that the use of operating windows facilitates the collaborative collection of information.

The overlap between the reaction, separation and apparatus operating windows determines the feasibility of a flowsheet (Schembecker and Tlatlik, 2003; Kiss, 2019). Tylko et al. (2006) provide a graphical description of the level of integration of functionalities based on the overlap of the reaction and separation windows (Figure S4.11, Supplementary Information). A downside of high integration of functionalities is the loss of degrees of freedom, such as requiring the reaction and separation pressures to be the same (Schembecker and Tlatlik, 2003; Tylko et al., 2006). Other trade-offs include increasing temperature to enhance the reaction, which could be detrimental to the catalyst (Hessel et al., 2014), and reducing pressures to avoid thermal degradation but requiring larger equipment (Kiss, 2019). The most common approach to expanding operating windows is to adjust operating conditions to create an intersection that can lead to a partially integrated configuration. For example, Steimel et al. (2013) proposed the introduction of a 'virtual' unit to change temperature or pressure to allow more overlapping between functions. Exploring more extreme process conditions, Hessel et al. (2014) proposed the 'novel process windows' concept that uses dimensions such as length and time and is particularly suited for microreactors and spinning disc reactors. Other efforts to expand operating windows of RD include additional driving forces (membranes), novel catalysts (enzymes) and alternative forms of energy (microwaves) (Werth et al., 2015).

Focusing on the development of generalised design tools for reactive-separation systems, an earlier attempt to tackle multicomponent systems is based on the element concept, proposed by Pérez Cisneros et al. (1997). The element concept considers repetitive parts of a molecule as one element, and these elements are used instead of components to find simultaneous chemical and physical equilibrium. Li et al. (2016) proposed a modified fixed-point method using the element concept as a simplification strategy to allow a graphical representation of systems containing four elements (which could include an inert) taking into consideration the

effects of temperature on reaction and separation. The modified fixed-point method is applied for conventional RD design, where input values such as operating pressure, Da number, inlet and outlet streams are required.

This work is the first to expand the boundaries of operating windows for RD by incorporating new features to assess ARDT and potential operating conditions in the early stages of process design. A simplification strategy termed ‘representative component’ is proposed to analyse multicomponent mixtures and identify the components that can potentially affect the operation. The vapour pressure curves of the lightest and heaviest representative components provide boundaries for the operating window. Another concept proposed to construct the operating window is the addition of a ‘sliding window’ of fixed width that moves along the temperature axis to mark potential operating points.

The basis for constructing the operating window comprises thermodynamic and kinetic data (e.g., vapour pressure, reaction rates), heuristics (e.g., avoid refrigeration) and constraints of material and experimental methods (e.g., degradation temperatures), previously proposed in a conceptual framework (Pazmiño-Mayorga et al., 2022a). Findings of operating windows include the identification of suitable ranges for operating conditions and insights to appraise ARDT during process synthesis. Results from the application of this study contribute to the development of novel efficient processes, while engineering time could be reduced by rapidly analysing the design space and providing initial values that could be used in detailed models, rigorous simulations or superstructure optimisation approaches.

Firstly, this paper briefly reviews five ARDT in scope. Then, it describes the construction of the operating window, including the selection of ‘representative components’ and the use of a ‘sliding window’. Finally, three case studies for methyl acetate production, lactic acid purification and tert-amyl methyl ether production demonstrate the application of operating windows.

4.4.2 Technical overview of advanced reactive distillation technologies

Reactive distillation is generally classified in the functional domain as an example of synergy generated by the combination of reaction and separation. Additional intensification features of ARDT provide new capabilities that can be categorised in other PI domains: spatial, temporal, thermodynamic and functional (Stankiewicz et al., 2019). Figure 4.4 highlights the additional governing PI domains for five ARDT, along with a brief description.

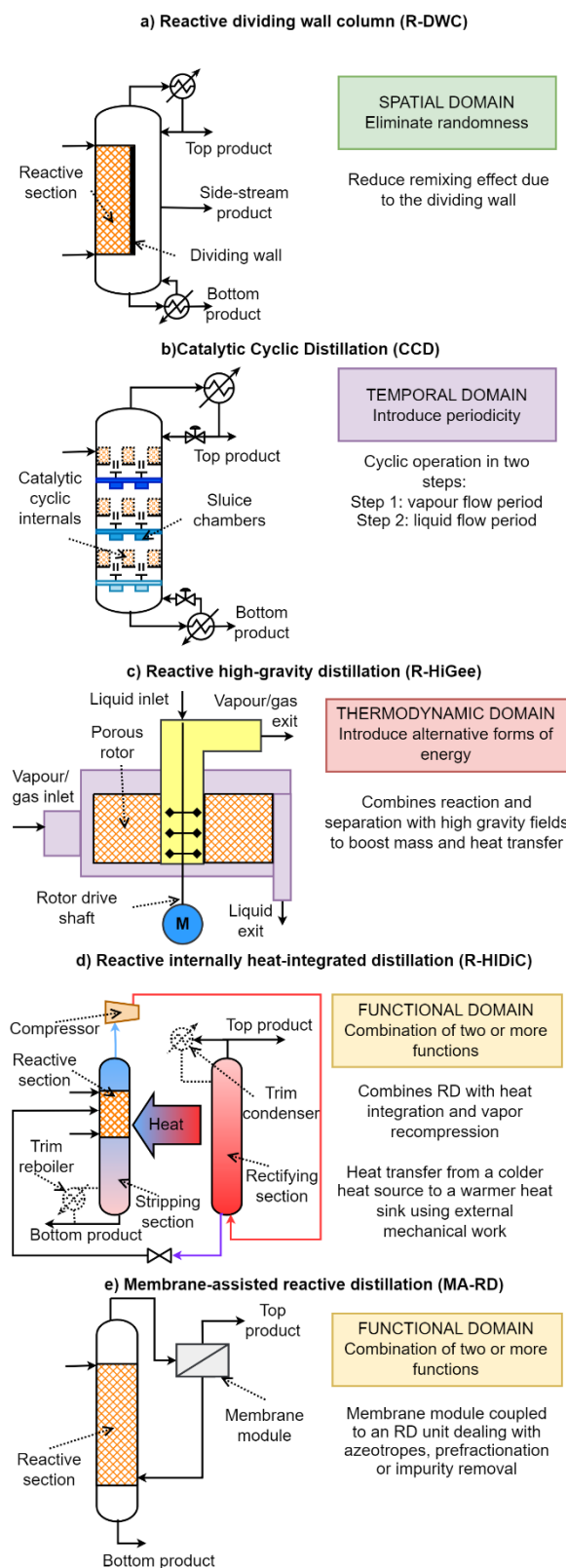


Figure 4.4. Advanced reactive distillation technologies and their governing process intensification domains (Adapted from Quaderer et al. (2000); Lutze and Gorak (2013); Kiss et al. (2019))

Key attributes of each advanced technology that could expand the applicability of RD are summarised as follows: a) In a reactive dividing-wall column (R-DWC), the location of a side stream in different stages allows the composition of the liquid phase to be adjusted, hence

changing the driving forces for reaction and separation. It also allows the recovery of unreacted components in side streams. b) In catalytic cyclic distillation (CCD), longer residence times can significantly help relatively slow reactions and operation at milder temperatures. c) In reactive high-gravity distillation (R-HiGee), short residence times can avoid undesirable series of reactions. d) In reactive internally heat-integrated distillation (R-HiDiC), the stripping section at low pressure (heat sink) and the rectifying section at high pressure (heat source) allow significant heat integration by partitioning and shifting the pressure window. e) In membrane-assisted reactive distillation (MA-RD), the membrane overcomes azeotropes or miscibility gaps to aid separation.

4.4.3 Methodology and approach

This section first proposes the 'representative components' and the 'sliding window' as new features to assess advanced reactive distillation technologies. Then, the procedure for building and interpreting the operating window over a temperature vs pressure diagram is presented. Finally, the scope and limitations of the proposed approach are noted.

4.4.3.1 New features for RD assessment using operating windows

4.4.3.1.1 Representative components

A new concept, 'representative components', is proposed to account for relevant species while facilitating analysis of process options because of the complexities of multicomponent mixture behaviour. In order to identify the 'representative components', three parameters are used for evaluation: nature of the component, amount, and vapour-liquid equilibrium data (if available). Finally, the lightest and heaviest 'representative components' are identified as the 'light representative' (LR) component and the 'heavy representative' (HR) component, respectively, whose vapour pressures provide boundaries to the operating window.

Nature of the component. Components in the feed and produced by reactions can interact. To find a balance between representing the complexity of a multicomponent system and ease of analysis, the nature of the component helps identify interactions (e.g., reaction, dilution) considering their potential effects. All the components participating in the system need to be identified and categorised as reactants, products, intermediate products, byproducts or impurities (whether reactive or inert) using the following guidelines:

- Reactants and products are those involved in the principal reaction, meaning that they are the basis to provide revenue, or they are the target components of the operation.

- Intermediate products occur when the main product is produced after a series of reactions. Therefore, intermediate products could be assumed to remain within the reaction-separation system and excluded from the composition of outlet streams. This is to ensure that intermediate products can be obtained in the liquid phase when producing the main product. A special case of intermediate products is when the forward and reverse reactions are needed in an equilibrium-limited reaction; hence the initial reactant is also the product of interest.
- Byproducts result from parallel or series reactions, which are typically undesired.
- Impurities can be identified as reactive or inert. When present in large quantities, they usually increase costs as larger equipment is needed and more energy is used for separation (Smith, 2016). Substituting for the complexity of multicomponent mixtures, some impurities could be discarded and lumped with others to denote a light inert, a heavy inert, or a potentially reactive component. Different scenarios could then be established to evaluate different assumptions (*e.g.*, stoichiometric vs excess reactant, partial vs complete conversion, side reactions, byproduct formation) because their interactions could influence the location of the operating window boundaries.

Amount of component. If byproducts or impurities are present in a relatively large amount to that of the main components, they are identified as representative components because of their potential impact on heating/cooling duties and the size of equipment. In contrast, if a component is expected to appear in a low quantity (*e.g.*, an inert trace component, a limiting reactant that is largely consumed or a byproduct of slow side reactions), its potential interactions need to be further evaluated using the vapour-liquid equilibrium criterion.

Vapour-liquid equilibrium. Gaseous components are disregarded when identifying the representative components because they are not likely to condense and only participate in the reaction while in the liquid phase and in contact with the catalyst. Therefore, the vapour pressure of a gaseous component does not provide boundaries for the region where liquid and vapour can coexist. Regardless of the nature and amount, the remaining components are evaluated to determine whether they affect the relative volatility (*e.g.*, promoting azeotropes). If so, these components are identified as representative components.

Selecting the light and heavy representative components. The decision-making flowchart in Figure 4.5 suggests how to identify the ‘representative components’. The lightest and heaviest are categorised as the ‘light representative (LR)’ and the ‘heavy representative (HR)’

components, respectively, whose vapour pressures provide boundaries for the operating windows. The identification of the light and heavy representative components is relevant because it allows an understanding of the complexity of the system and then facilitates a more accessible representation for further analysis. As such, the temperature difference between the LR and HR components defined for a reference pressure (denoted by ΔT_b) becomes characteristic of the chemical system. The ΔT_b can provide a benchmark to construct the operating window (i.e., sliding window in the next section), identify the hot and cold boundaries of the system and guide the selection of technology. The procedure for identifying the representative components uses three relevant characteristics: nature of the component, amount, and vapour-liquid equilibrium data. Note that other issues such as thermal and chemical stability and safety hazards are not considered; therefore, constraints related to materials and experimental methods are introduced later.

4.4.3.1.2 Sliding window

The 'sliding window' concept is drawn from the idea of a window containing two panels, one fixed and the other that slides horizontally. The value of ΔT_b defines the width of the sliding window, as illustrated in Figure S4.12 in the Supplementary Information. The intersection of the sides with the vapour pressure curve of the light (or heavy) representative components allows the detection of suitable operating points. The ΔT_b is important because it is characteristic of the chemical system and could be used while searching for suitable operating regions for reaction and separation.

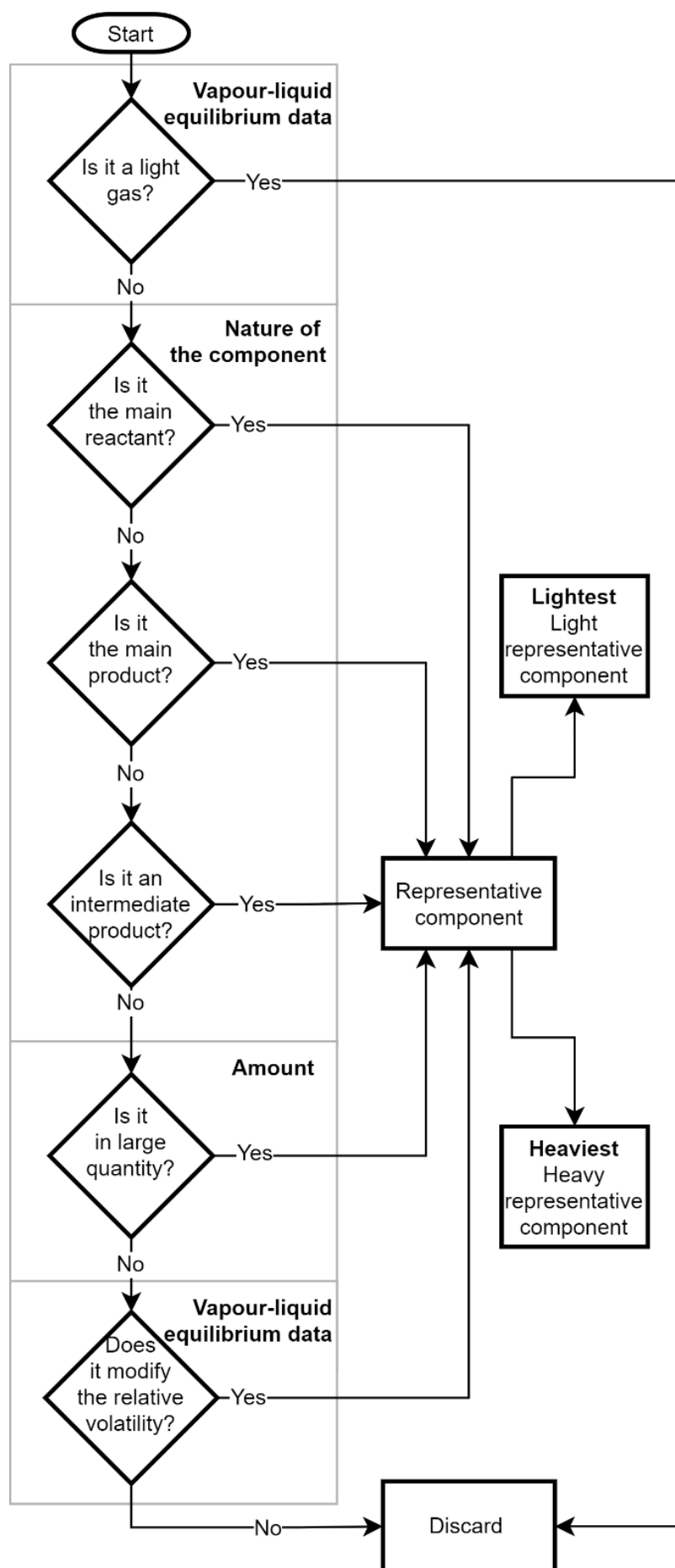


Figure 4.5. Flowchart to identify the representative components

4.4.3.2 Operating windows to evaluate advanced reactive distillation technologies

4.4.3.2.1 Input data required to construct the operating windows

Physical property data for the components in the chemical system. The driving force for separation in distillation is the difference in volatility of different components. The volatility is characterised by the K-values of each component, which depends on pressure and temperature. Thus, boiling points can be used as a proxy to assess the ease of separation. Initially, boiling points at a single pressure (e.g., atmospheric or other reference pressure) are collected to facilitate analysis, arranging the components in order of increasing boiling point. For non-ideal systems, the order may change with pressure. Therefore, this step may need to be revisited later if a different pressure is identified as more suitable. Vapour pressure data at different temperatures are collected for the light and heavy representative components. These values provide boundaries for the region where liquid and vapour coexist and separation could occur. The critical temperature and pressure provide boundaries for the operating window only when the operating points are located near the critical region. Otherwise, these boundaries are not relevant.

Kinetic parameters for the main and side reactions. According to Arrhenius's law, reaction rates depend heavily on temperature. This is relevant for liquid phase reactions involved in RD because of the overlap needed with the separation window. A special case considered in this work is the occurrence of undesired side reactions, which need to be prevented. During process synthesis, obtaining kinetic data is challenging because of the variables involved (e.g., catalyst type and formulation, experimental conditions) and the variety of experimental methods, analytical techniques and regression models used. As a result, kinetic parameters can be expressed in different dimensions or bases, making comparison difficult. To represent the main and side reactions in the construction of the operating window, the reaction rate constant is selected using the mass of catalyst as a basis to facilitate comparison. Kinetic parameters – pre-exponential factor and activation energy – are used to determine the reaction rate constant at different temperatures. Reaction rate constants for the main and side reactions are plotted using a secondary vertical axis when building the operating windows. An intersection between the reaction rate curves could help identify a temperature boundary to enhance the main reaction while preventing byproduct formation.

Material constraints and limitations of experimental methods. In addition to the separation and reaction windows, thermal resistance and pressure rating of materials must be considered

when constructing the operating windows. Here, materials refer to the components (e.g., reactants, products), catalysts and materials of construction (e.g., for vessels, column internals, membranes). Thermal degradation (or decomposition) is evaluated experimentally. For commercial catalysts, the decomposition temperature is usually provided by the vendor. For catalysts under development and chemical compounds, thermal decomposition studies could provide a reference degradation temperature. In terms of the operating window, this means that the lowest degradation temperature in the system restricts the operating points. To identify the operating limits for materials of construction, process design guidelines are used (e.g., operating pressure between 1 and 10 bar, temperatures between 40 and 260°C) (Turton, 2018). Operation outside these ranges is possible, but operational and economic trade-offs need to be considered. In addition, atmospheric pressure is denoted on the operating window because it facilitates identifying restrictions to operate under vacuum. Among the technologies evaluated, CCD cannot operate below atmospheric pressure due to restrictions inherent to the construction and operation of the internals (Kiss, 2013; Maleta et al., 2015). The design of internals for HiDiC might constrain pressure drop allowances; however, vacuum operation could be performed (Campbell et al., 2008). Experimental methods constraints involve models used to describe kinetics and phase equilibria. These models are typically produced following laboratory procedures within a range of validity (e.g., temperature, concentration). Working outside these ranges could lead to unfeasible operating points, hence providing misleading outcomes to guide the selection of technologies.

4.4.3.2.2 Construction of the operating windows

Relationship between the input data and a systematic guide for constructing the operating window is explained graphically in Figure S4.13 in the Supplementary Information, and the main features of the operating window are illustrated in Figure 4.6.

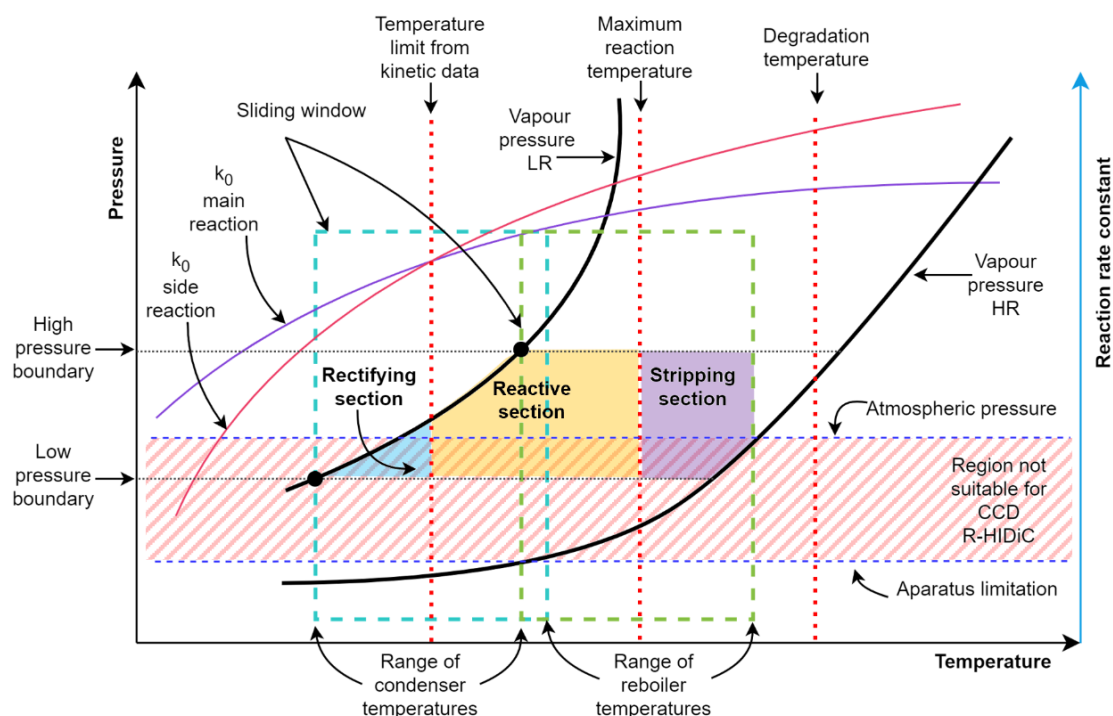


Figure 4.6. Main features of the operating windows

Once the information regarding the system is gathered, vapour pressures of the light and heavy representative components are plotted over the temperature vs pressure diagram. Points between these two curves represent conditions where vapour-liquid separation could complement a liquid-phase reaction. Critical temperature and pressure could be added if necessary.

A secondary axis is used to represent the reaction rate constant of the most relevant main and side reactions. This is important because a temperature limit where one reaction is enhanced over the other could be identified, which would suggest potential boundaries for the reaction window. This limit is represented as a vertical line at the intersection between the two reaction rate curves indicating the temperature where a shift occurs.

Materials constraints and experimental method limits are presented as straight lines. Vertical lines indicate the degradation temperature for the catalyst or components and the range of validity of models to estimate vapour pressures or reaction kinetics. Horizontal straight lines denote operation above and below atmospheric conditions or limitations of the apparatus.

The sliding window – a dashed box with two panels – moves along the temperature axis. The location of the left side is set by the use of cooling water at approximately 20 to 30°C, which is orders of magnitude cheaper than refrigeration, whereas the right side aims to avoid thermal degradation while using typical steam levels: low-pressure steam (3–6 bar) at 120 to 150°C, medium-pressure steam (10 bar) at 180°C and high-pressure steam (40–50 bar) at 250

to 265°C (Smith, 2016). The flowchart and explanation in Figure S4.14 in the Supplementary Information provide further information.

Finally, the operating window is presented as a shaded region in Figure 4.6, including the main features providing boundaries and regions that could aid the selection of technologies. Values for operating conditions that can be read from the operating window are:

- Operating pressure: Found at the intersection of the left side of the window and the vapour pressure curve of the light representative component.
- Condenser temperature: Typically, this value lies between 40 and 60°C based on the use of cooling water unless an alternative boundary is more favourable.
- Reboiler temperature: Typically, this value lies between 150 and 245°C based on the use of different steam levels unless the degradation temperature of a component provides a boundary at a lower temperature.
- Maximum temperature in the reactive section: Defined by the degradation temperature of the catalyst, or the thermal degradation of a component (if lower than the former).
- Rectifying and stripping sections: Identified towards the cold and hot ends of the window. The reactive section could be located in either or both sections.

A special case, when ΔT_b is less than 60°C, can exploit vapour recompression within economic limits for non-reactive HIDIc (Kiss and Olujić, 2014). This heuristic is extended to assess R-HIDIc by using two sliding windows at different pressures to identify a stripping section bounded by a low pressure and a rectifying section by a high pressure. The right side of the first sliding window – to locate the stripping section – uses the intersection between atmospheric pressure and the vapour pressure of the heavy representative component. To locate the rectifying section, a second sliding window is defined by applying a pressure ratio of 1.3–3 to avoid excessive compression costs (Suphanit, 2010). A detailed flowchart for the location of the two sliding windows is shown in Figure S4.15 in the Supplementary Information. The operating conditions that could be identified from the two operating windows are:

- The stripping section at low pressure is associated with the reboiler temperature to complement heating, if required.
- The rectifying section at high pressure is associated with the condenser temperature to complement additional cooling.
- The reactive section is identified using the degradation temperature boundaries.

These operating conditions can be used to initialise detailed models to assess the performance of a technology in a later stage of process design.

4.4.3.3 Scope and limitations of operating windows

This paper investigates operating windows to expand the applicability of reactive distillation through advanced technologies, focusing on systems featuring an equilibrium-limited reaction in the liquid phase or fast solid-catalysed reactions where a stripping gas reacts in the liquid phase, and rapid removal of reaction products is needed. A special application for fluid separations occurs when adding a suitable ‘reactive separating agent’ – analogous to a mass separating agent typically used in separations – that promotes an equilibrium-limited reaction that facilitates the separation.

Considerations that are not captured when constructing operating windows include the inability to explore heat integration opportunities (Steimel et al., 2014), miscibility information (particularly for liquid-liquid systems) and economic assessment (Kraume et al., 2022). Also, the application of operating windows is typically limited to processes without recycles (Recker et al., 2015; Steimel et al., 2013), hence the iterative nature of the procedure to devise a feasible solution (Schembecker and Tlatlik, 2003). The proposed methodology does not cover the potential for foaming, corrosion and polymerisation, which could be assessed in a later stage of detailed design. Collectively, the technical feasibility and economic benefit of a configuration elucidated in an operating window are not guaranteed, hence the need for further evaluation of the overall process performance.

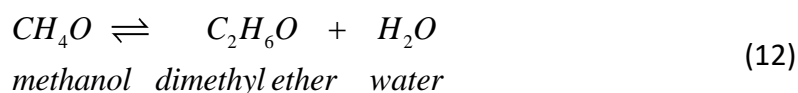
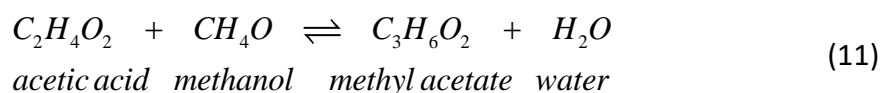
4.4.4 Case studies to illustrate the construction of operating windows

Three case studies are used to demonstrate the proposed approach. Basic information data, boiling points and critical properties may be retrieved from Aspen Plus databanks. Details are presented in the Supplementary Information. To provide a simple way to verify the outcomes of the operating windows, results from studies in the literature are used for comparison. Single values from various experimental, modelling, simulation and optimisation studies are compared with the range of operating bounds found from the operating windows. This is particularly relevant for novel technologies where pilot or industrial scale data are sparse, and isolated efforts studying individual technologies were not clearly linked to process synthesis.

4.4.4.1 Case study 1: Methyl acetate production

4.4.4.1.1 Description of the methyl acetate system

Methyl acetate production represents an industrially relevant esterification process with azeotrope formation, which has been widely studied. Methyl acetate is the lightest organic ester, soluble in most common organic solvents. Applications include use as a process solvent and precursor in the synthesis of pharmaceutical intermediates (Berre et al., 2014). Eastman developed industrial production of methyl acetate production by RD in the early 1990s. This case study explores the esterification of methanol and acetic acid using a solid catalyst (Amberlyst 15). The feeds are pure acetic acid and methanol. Reactions involved in the system include the esterification of acetic acid with methanol (11) and the dehydration of methanol into dimethyl ether (DME) (12). Table S4.10 in the Supplementary Information presents the kinetic parameters for both reactions. The component in the system exhibits two low boiling azeotropes: methyl acetate–methanol and methyl acetate–water. The ester product is usually removed as the methanol–methyl acetate azeotrope that needs further processing. Methyl acetate is sold at different specifications (97%wt., 99.5%wt., 95%wt.) depending on the application (Wacker, 2022).



4.4.4.1.2 Operating windows applied to methyl acetate production

Table 4.3 presents basic property data and the nature of the five components in the system, listed in increasing boiling point order. DME is not identified as a representative component due to its low boiling point. The next low-boiling component, methyl acetate, is identified as the light representative component, while acetic acid is the heavy representative component. The reaction rate constant for DME production is lower than that for methyl acetate; hence the reaction rate curve for the side reaction briefly appears in Figure 4.7, indicating that DME will form at low rates. Additional boundaries are the degradation temperatures of the catalyst at 120°C and of acetic acid at 230°C. As a result, 120°C is the maximum reaction temperature, although separation could occur at higher temperatures. The temperature difference between methyl acetate and acetic acid is approximately 61°C. The left side of the sliding window (represented with a vertical dashed line in Figure 4.7) starts at 40°C and moves up to

60°C. The final position of the right side is the maximum reaction temperature (120°C). However, the sliding window can still move rightwards because higher temperatures could be exploited for separation only, for example, up to 160°C, so that low-pressure steam can be used.

Table 4.3. Methyl acetate production: basic property data and nature of the components

Components	Nature	NBP (°C)	Critical Temperature (°C)	Critical Pressure (atm)	Degradation temperature (°C)
Dimethyl ether	Byproduct	-24.8	127.9	53.3	-
Methyl acetate (LR)	Product	56.9	233.4	46.9	727 ^a
Methanol	Reactant	64.7	239.4	79.8	-
Water	Byproduct	100.0	373.9	217.8	-
Acetic acid (HR)	Reactant	117.9	318.8	57.1	230 ^b

^a Porterfield et al.(2017), ^b Li et al. (2017)

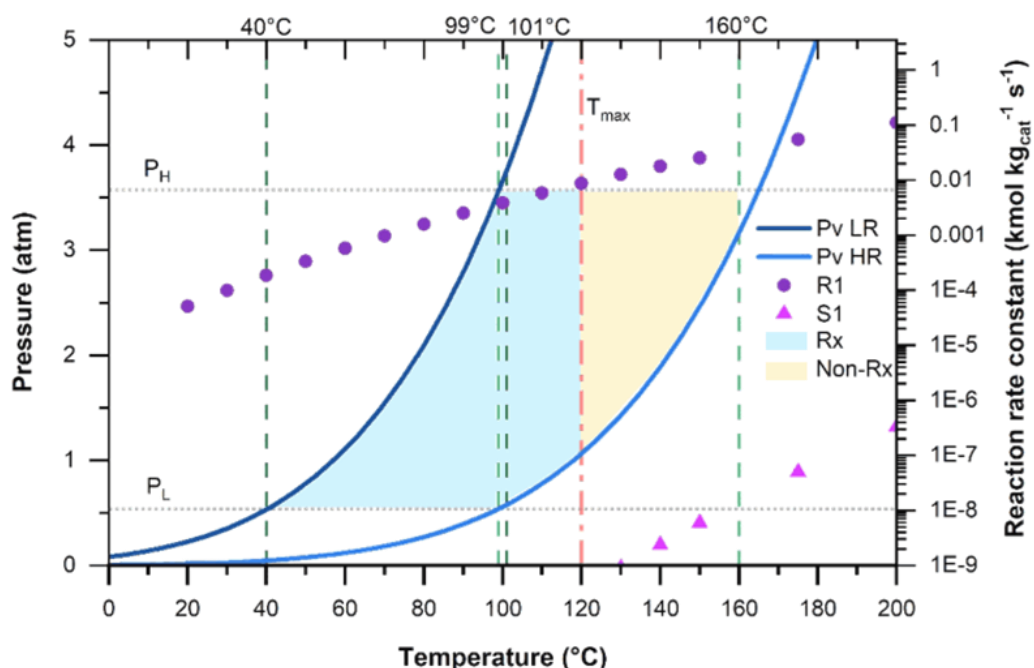


Figure 4.7. Operating windows for the methyl acetate system (Pv LR: vapour pressure of the light representative component, Pv HR: vapour pressure of the heavy representative component, R1: reaction rate constant for main reaction, S1: reaction rate constant for side reaction, Rx: reactive zone, non-Rx: non-reactive zone, PH: high-pressure boundary, PL: low-pressure boundary, Tmax: maximum reaction temperature)

The intersection between the vapour pressure curve of the light representative component and the left sides of the sliding window suggests a range of operating pressure between 0.53 and 3.57 atm. The condenser temperature ranges from 40 to 99°C, and the reboiler temperature from 101 to 160°C. All boundaries needed to identify the operating window are shown in Figure 4.7, where the reactive and non-reactive sections are shaded. The operating bounds for the methyl acetate system are summarised in Table 4.4.

Table 4.4. Operating bounds for the production of methyl acetate

Parameter	Units	Value
Operating pressure	atm	0.53 – 3.57
Condenser temperature	°C	40 – 99
Reboiler temperature	°C	101 – 160
Maximum reaction temperature	°C	120

4.4.4.1.3 Verifying operating bounds for the methyl acetate system

The results of this case study indicate that simultaneous reaction and separation for methyl acetate production can be carried out under conventional operating conditions, with only part of the range of pressures requiring vacuum. These findings, while preliminary, provide initial estimations about utilities and construction arrangements that may be considered in detailed designs. In addition, an opportunity to expand the reaction window is easily identified in Figure 4.7, where catalysts offering greater thermal stability could shift the temperature limit imposed by degradation. The operating bounds found are consistent with the pressure of 1.2 atm reported by Al-Arfaj and Luyben (2002), while Pöpkén et al. (2001) used pressures of 0.2 to 0.98 atm. In the latter case, the lower boundary is slightly outside of the suggested range and may need the use of a cold utility supplied at 8°C, assuming a minimum temperature approach of 10°C. Setting the operating pressure to atmospheric is preferred for distillation; hence other studies reported atmospheric pressure for an RD unit with extractive distillation (Zuo et al., 2014), a reactive dividing wall column (An et al., 2015) and membrane-assisted RD (Babi et al., 2014). It is easily identified from Figure 4.7 that using atmospheric pressure allows the use of cooling water. No published studies are known to have considered R-HIDiC. However, as ΔT_b is close to the 60°C limit, the potential of exploiting R-HIDiC using two different pressures is presented in the Supplementary Information.

Comparison of the operating bounds found with the operating points identified in studies focusing on conventional RD and ARDT confirms that the proposed approach allows the identification of operating points using readily available information of a well-studied chemical system. At the same time, opportunities to expand the operating window are easily identified even though the industrial process is well established.

4.4.4.2 Case study 2: Lactic acid concentration and purification

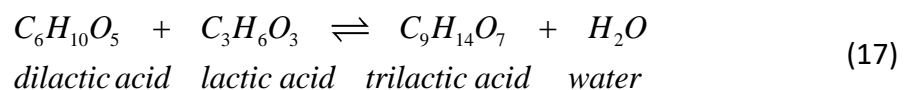
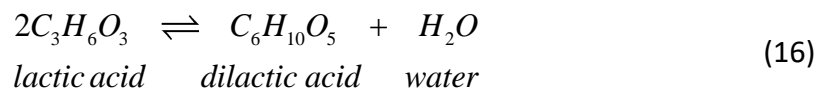
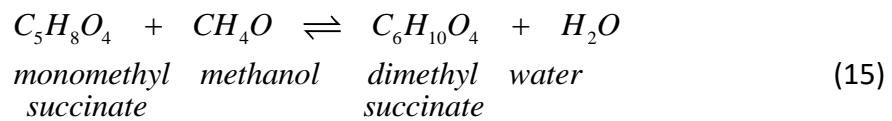
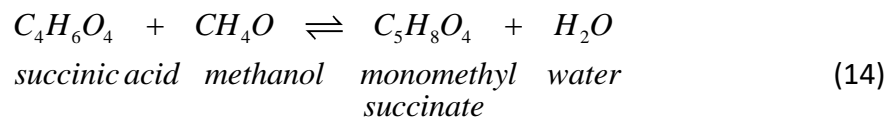
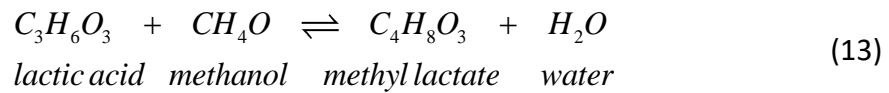
4.4.4.2.1 Description of the lactic acid system

Lactic acid is a bi-functional molecule highly soluble in water with many commercial applications, including food, pharmaceuticals, personal care, biodegradable polymers and as

a building block molecule (Miller et al., 2017). The most common route to produce lactic acid is the biotechnological fermentation of sugars with microorganisms (Alves de Oliveira et al., 2018). Downstream processing of the fermentation broth includes liquid-liquid extraction, membranes with electrodialysis and anion exchange to remove residual sugars and organic nitrogen (Khunnonkwao et al., 2012; Starr and Westhoff, 2014). A dilute aqueous solution containing lactic acid and other organic acids needs to be purified. This feed is considered a candidate for RD because an esterification reaction can be promoted by adding alcohol (a reactive separating agent), and then esters can be separated more easily than their corresponding acids (Joglekar et al., 2006).

This case study considers a dilute aqueous mixture containing lactic acid and succinic acid, a reactive impurity. The esterification reaction is promoted by methanol using a solid catalyst (Amberlyst 35). Once the heavier succinates are removed by separation, methyl lactate is hydrolysed into the acid form to obtain food-grade lactic acid at 88 %wt.

This system features the following reactions: esterification of lactic acid (13), esterification of succinic acid into monomethyl succinate (14) and dimethyl succinate (15) and oligomerisation of lactic acid into dilactic acid (16) and trilactic acid (17).



4.4.4.2.2 Operating windows applied to lactic acid concentration and purification

The system consists of eight species listed in increasing boiling point order in Table 4.5, together with their nature, critical properties, and degradation temperature. The process needs to promote, separately, both the forward and reverse reactions. Therefore, lactic acid is characterised as both reactant (for esterification) and product (of hydrolysis), while methyl

lactate is an intermediate product. In addition, water contained in the feed mixture is identified as an impurity that is also produced in the esterification reaction. When identifying the representative components, succinic acid, a heavy impurity, is present in small quantities and does not modify the relative volatility of the mixture, so it is not included among the representative components. The oligomers of lactic acid – byproducts – are likely to appear in low quantities and are therefore excluded from the list of representative components. Finally, monomethyl and dimethyl succinates (MMS & DMS) are identified as representative components because they form azeotropes with lactic acid, although they are likely to appear in low quantities. Hence the LR and HR components are methanol and MMS, respectively. However, MMS is not well documented: its property data are scarce. Therefore, lactic acid – the second heaviest representative component – and methanol are used to provide boundaries to the operating window as heavy and light representative components, respectively. The temperature difference between methanol and lactic acid at atmospheric pressure is 152°C. The kinetics parameters for the system are listed in Table S4.11 (Supplementary Information). The main reaction for the production of methyl lactate production is plotted in the operating window diagram (Figure 4.8), together with the side reaction for the formation of MMS, because the latter is the first parallel reaction that competes to consume methanol. The intersection between the curves representing the reaction rate constant for the main and side reactions produces a temperature limit of 190°C, above which side reactions are enhanced.

Table 4.5. Lactic acid purification: basic property data and nature of the components

Components	Nature	NBP (°C)	Critical Temperature (°C)	Critical Pressure (atm)	Degradation temperature (°C)
Methanol (LR)	Reactant	64.5	239.4	79.8	–
Water	Reactive impurity/Intermediate product	100.0	373.9	217.8	–
Methyl lactate	Intermediate product	144.8	334.2	41.8	–
Dimethyl succinate	Byproduct	196.4	383.9	32.4	–
Dilactic acid	Byproduct	215.9	386.9	34.3	–
Lactic acid (HR)	Reactant/Product	216.6	401.9	58.8	–
Monomethyl succinate	Byproduct	222.9	409.9	38.4	–
Succinic acid	Reactive impurity	317.6	564.9	49.3	235 ^a
Trilactic acid	Byproduct	345.9	503.9	25.2	–

^a Smith and Hong-Shum (2003)

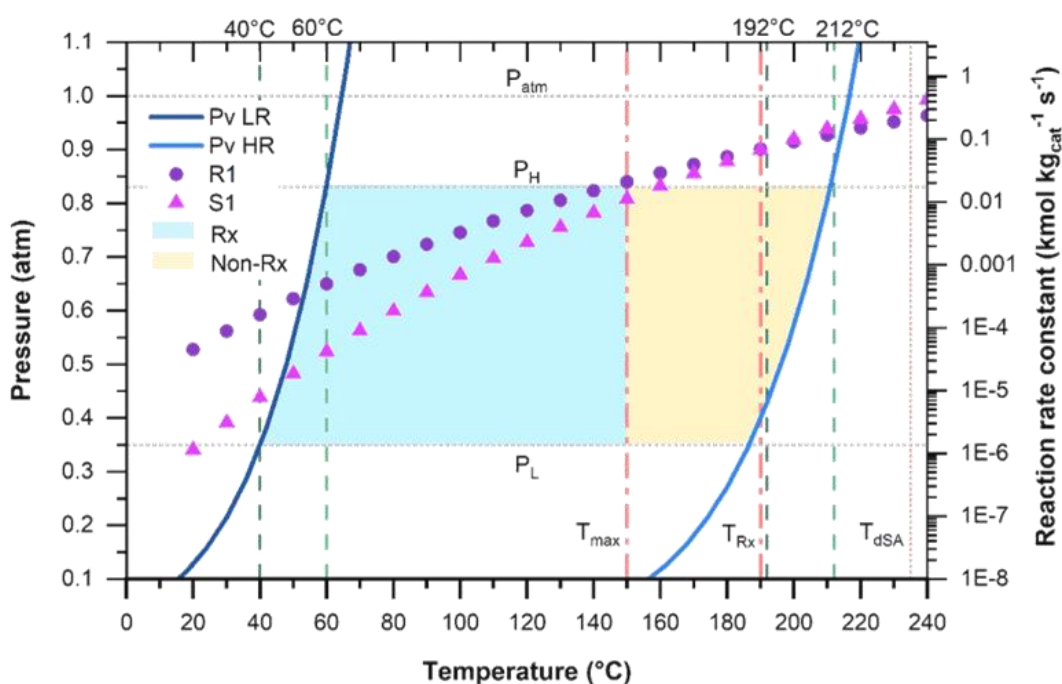


Figure 4.8. Operating window for the lactic acid system (P_{atm} : atmospheric pressure, T_{Rx} : temperature limit for reactions, T_{dSA} : degradation temperature of succinic acid)

Regarding material constraints, the degradation temperature of the catalyst (150°C) and succinic acid (235°C) are represented in the diagram. Therefore, the maximum reaction temperature is 150°C, but separation could occur at higher temperatures. The sliding window has a width of 152°C, the boiling point difference between methanol and lactic acid. The left side moves from 40 to 60°C. The right side exceeds the maximum reaction temperature but marks a temperature below the degradation temperature of succinic acid. These limits define the operating window, as shown in Figure 4.8. The operating bounds obtained from the operating window are summarised in Table 4.6. The temperature limit for the reactive section is 150°C, while the temperature range is 40–60°C for the condenser and 192–212°C for the reboiler. Pressures below the atmospheric are required to avoid exceeding temperature limits.

Table 4.6. Operating bounds for the concentration of lactic acid

Parameter	Units	Value
Operating pressure	atm	0.35 – 0.83
Condenser temperature	°C	40 – 60
Reboiler temperature	°C	192 – 212
Maximum reaction temperature	°C	150

4.4.4.2.3 Verifying operating bounds for the lactic acid system

An initial objective was to identify guidelines for the selection of technologies. An important finding that contributes to this objective is that the range of operating pressures identified suggests operation at vacuum conditions only. Following Figure 4.6, suitable technologies could include R-DWC, R-HiGee and MA-RD. Another finding indicates that the temperature limit where the side reaction is enhanced over the main reaction lies inside the separation window. This observation is important because it could have implications when operation at higher temperatures is possible in case catalysts with better thermal resistance are available. Regarding limitations due to the unavailability of data, using lactic acid as the light representative component instead of MMS allowed the operating bounds to be identified. This case study was successful as it was able to identify the ranges of operating conditions despite of missing information, and the results are verified with studies from the literature. Our previous study for the conceptual design of a dual R-DWC accounted for succinic acid as a reactive impurity and temperature limits to avoid lactic acid and succinic acid degradation (Pazmiño-Mayorga et al., 2021). The operating pressure selected after a sensitivity analysis was 0.5 atm, and the condenser and reboiler temperatures were 58°C and 183°C, respectively. These results lie within the range of operating conditions identified in this work.

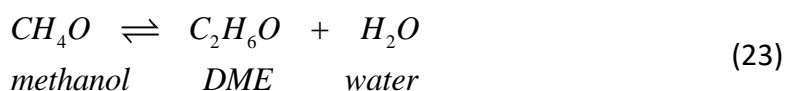
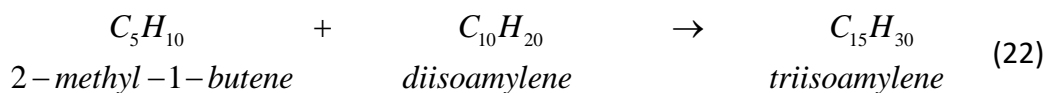
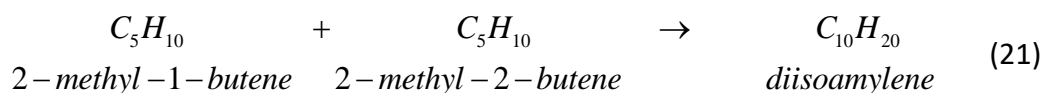
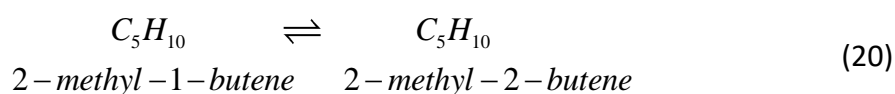
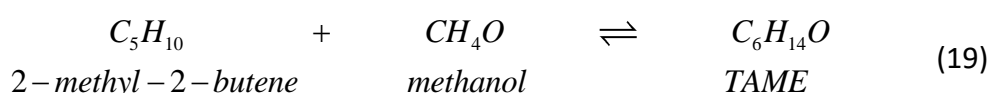
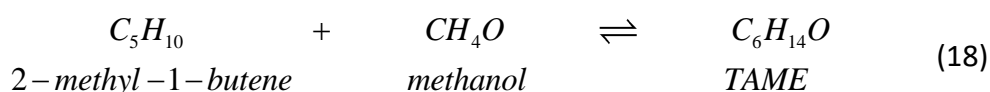
Other simulation studies for the purification of lactic acid accounted for complex feed mixtures containing succinic acid, but they dismissed the effect of the esterification of succinic acid (Su et al., 2013; Kim et al., 2017). Su et al. (2013) evaluated a sequence of reactive and conventional distillation columns. The operating pressure for the RD column performing esterification is ~0.2 atm, and the distillate temperature reported is 39°C. These set of results must be interpreted with caution as they cannot be read from the operating window, as the composition of the distillate stream is a mixture of methanol, water and methyl lactate. The reboiler temperature slightly exceeds the degradation temperature of succinic acid, although a temperature of 105°C is set for the lowest reactive stage as a design specification. Kim et al. (2017) presented partially and fully thermally coupled configurations, where the latter is equivalent to a reactive dividing wall column. The operating pressure for the esterification section is 1 bar, and the reboiler temperature is ~230°C. The operating conditions of these two studies are outside the ranges obtained in this work. This discrepancy could be attributed to the effect of how byproducts are distributed in the outlet streams and the degradation temperature of succinic acid, which was not considered. Most operation bounds identified in

the operating window are related to temperature constraints, which suggest that prior knowledge of the system (e.g., physiochemical properties, degradation temperatures) is fundamental to identifying feasible regions of operation. The results of this case study suggest that data of a well-studied compound could replace those of poorly characterised species to allow analysis in the event that reliable data is not available.

4.4.4.3 Case study 3: Tert-amyl methyl ether production

4.4.4.3.1 Description of the tert-amyl methyl ether system

Tert-amyl methyl ether (TAME) is a fuel additive produced by addition of isoamylenes to methanol using two reactors and a methanol recovery unit (Marcilly, 2005). The feed to the process is produced in the FCC unit of a petroleum refinery, which contains isoamylenes in significant quantities, inert alkanes, olefins, cyclic components from C5 to C8 and sulphur (Klöker et al., 2003). This system features three main reactions that are equilibrium-limited and include the TAME production from isoamylenes 2M1B (18) and 2M2B (19) and one isomerisation reaction between 2M1B and 2M2B (20) (Luyben and Yu, 2008). Possible side reactions include the formation of dimers (21) and trimers (22) of 2M1B and 2M2B (Cruz et al., 2007) and methanol condensation to dimethyl ether (23) (Subawalla and Fair, 1999). The reactions are catalysed by a solid catalyst (Amberlyst 35). Table S4.12 in the Supplementary Information presents the kinetic parameters for the main and side reactions.



The mixture of reactants, products and inerts exhibits minimum-boiling azeotropes, mostly between methanol and inerts entering with the feed (Subawalla and Fair, 1999). TAME purity

is typically larger than 96% wt., but it could also be used as a hydrocarbon mixture containing between 10 and 30 % wt. (European Commission, 2006). In this work, the feed is specified using three non-reactive impurities: lightest and heaviest alkanes (i.e., isopentane, cyclopentane) and one alkene (1-pentene), following the approach of Klöcker et al. (2003). This approach allows accounting for a realistic feed containing ~70% inerts, which will affect energy use and equipment size. Furthermore, side reactions – usually dismissed in simulation studies – and unwanted byproducts may have an effect, which will be evaluated using two scenarios: Scenario 1 ignores side reactions, while Scenario 2 takes them into account.

4.4.4.3.2 Scenario 1: TAME production disregarding side reactions

Table 4.7 presents the basic properties and the nature of the components, listed in normal boiling point order. Reactants and the product are identified as representative components, along with all inerts, because they account for a large proportion of the feed. The lightest and heaviest components of the system (isopentane and TAME) are the LR and HR components, respectively, whose temperature difference is slightly below 60°C. Thus, a special case with two sliding windows is analysed to identify regions where the rectifying and stripping sections of an R-HiDiC could operate. The right side of the first sliding window – to identify the stripping section – is located at the intersection of the vapour pressure curve of the heavy representative component and pressure of 1 atm. The corresponding temperature is 87°C, and the left side marks 28°C. Then, the sliding window moves horizontally, adding the value of ΔT_b , which corresponds to 145°C (Figure 4.9, a). The temperature bounds for the reboiler temperature are 28 and 145°C. The intersections of the leftmost and rightmost sides of the sliding window with the vapour pressure curve of the heavy representative component mark 0.11 and 4.4 atm as the pressure bounds for the low-pressure stripping section.

Table 4.7. Scenario 1 for TAME production: basic property data and nature of the components

Components	Nature	NBP (°C)	Critical Temp. (°C)	Critical Press. (atm)	Degradation temperature (°C)
Isopentane (LR)	Inert impurity	27.8	187.3	33.4	–
1-pentene	Inert impurity	30.1	191.7	35.1	–
2M1B	Reactant	31.2	191.9	34.0	–
2M2B	Reactant	38.5	196.9	33.8	–
Cyclopentane	Inert impurity	49.3	238.6	44.5	–
Methanol	Reactant	64.7	239.4	79.8	–
TAME (HR)	Product	86.4	260.9	30.0	326.9 ^a

^a Morton et al. (2011)

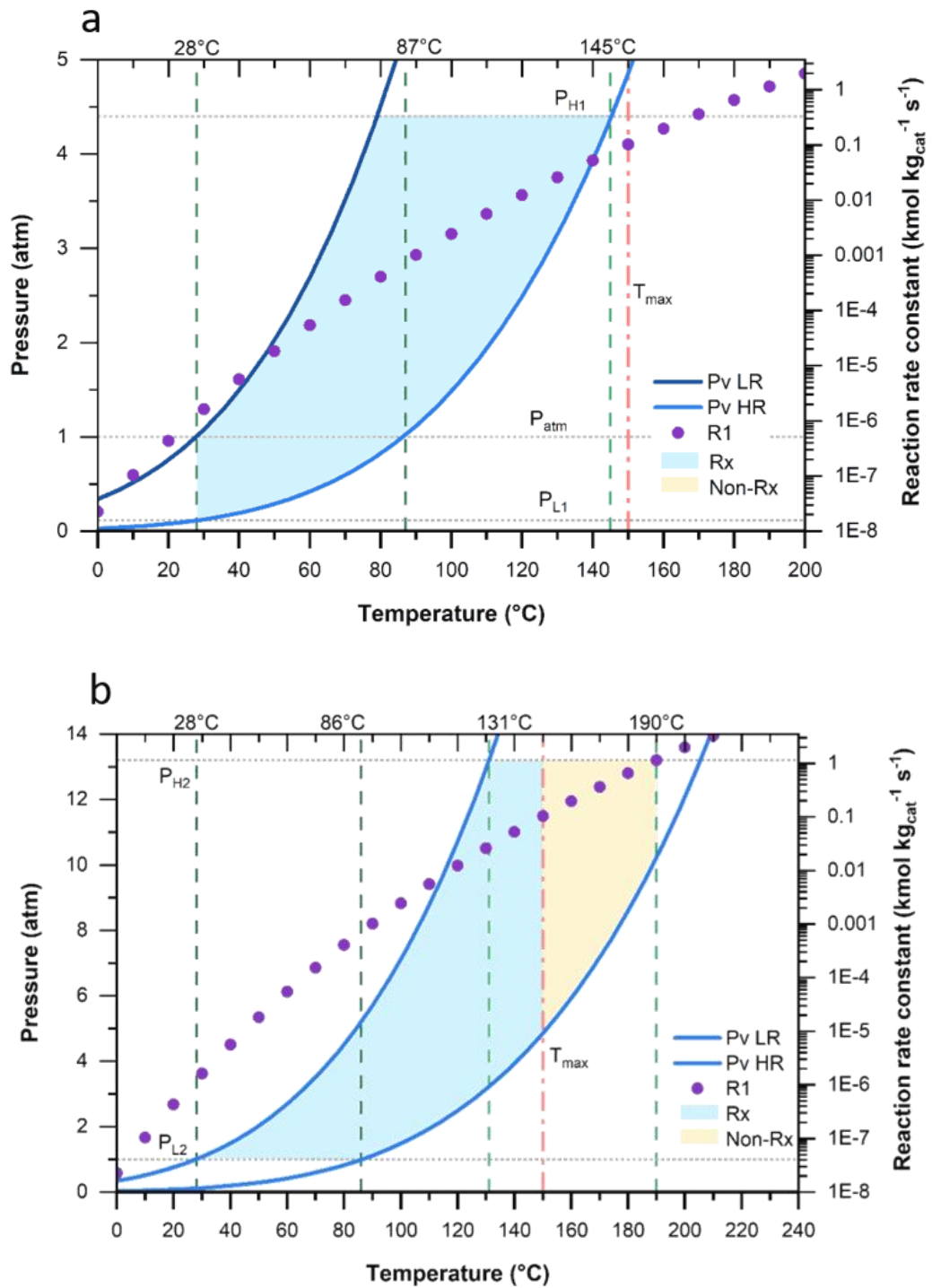


Figure 4.9. TAME case (Scenario 1): operating windows for the low-pressure stripping section (a) and high-pressure rectifying section (b) (P_{H1}: high-pressure boundary for the stripping section, P_{L1}: low-pressure boundary for the stripping section, P_{H1}: high-pressure boundary for the rectifying section, P_{L1}: low-pressure boundary for the rectifying section)

For the rectifying section, the left side of the second sliding window is positioned at the intersection of the vapour pressure curve of the light representative component and 1 atm (minimum value assumed for the high-pressure section). Then, the window slides up to the intersection of the vapour pressure curve of the light representative component and 13.2 atm (calculated using a compression ratio of 3) (Figure 4.9, b). The condenser temperature bounds

are 28 and 131°C, identified by the intersection of the vapour pressure curve of the light representative component and the left sides of the second sliding window.

The degradation temperature of the catalyst divides the operating window into a region where reaction and separation can take place below 150°C, and temperatures up to 190°C could be used for separation only. The reactive zone could be located in either section of the R-HiDiC. However, the reaction rate constant data for etherification of 2M2B indicates that higher temperatures favour the reaction. Thus, the reactive section is more likely to be in the high-pressure rectifying section.

4.4.4.3.3 Scenario 2: TAME production considering side reactions

Although the occurrence of side reactions during the production of TAME is acknowledged, the unavailability of kinetic parameters has limited their inclusion in simulation-based studies (Subawalla and Fair, 1999; Vanaki and Eslamloueyan, 2012). Kinetic studies focusing only on oligomerisation reactions (Cruz et al., 2006, 2007) and DME production (Kiviranta-Pääkkönen et al., 1998) are used to explore the effect of side reactions in Scenario 2. To exemplify the effect of additional byproducts, two oligomers are selected based on the availability of thermodynamic data: the dimer 2,3,4,4-tetramethyl-1-hexene and the trimer 2,4,6,6,7,7-hexamethylnon-3-ene. Byproducts from methanol condensation are dimethyl ether and water. The kinetic parameters are presented in Table S4.12 in the Supplementary Information. Table 4.8 lists the components – including byproducts of the side reactions – and their nature. DME is likely to form at low rates due to the large activation energy, so water content will be low too. The pre-exponential factors suggest that the oligomerisation reactions are slower than the main reactions. Therefore, the rate of formation of byproducts is expected to be low, so byproducts are not considered when selecting representative components. Thus, isopentane and TAME are defined as the light and heavy representative components, respectively.

The reaction rate constants for 2M2B etherification and triisomylenes production are the largest among the main and side reactions; these are represented using the secondary vertical axis in Figure. Note that temperatures below approximately 110°C favour the side reaction (S1) over the main reaction (R1). Therefore, a vertical temperature boundary is defined where the rate constant curves intersect to promote the main reaction.

Table 4.8. Scenario 2 for TAME production: basic property data and nature of the components

Components	Nature	NBP (°C)	Critical Temperature (°C)	Critical Pressure (atm)	Degradation temperature (°C)
DME	Byproduct	-24.8	127.0	53.0	—
Isopentane (LR)	Inert impurity	27.8	187.3	33.4	—
1-pentene	Inert impurity	30.1	191.7	35.1	—
2M1B	Reactant	31.2	191.9	34.0	—
2M2B	Reactant	38.6	196.9	33.8	—
Cyclopentane	Inert impurity	49.3	238.6	44.5	275.0 ^a
Methanol	Reactant	64.7	239.4	79.8	—
TAME (HR)	Product	86.4	260.9	30.0	—
Water	Byproduct	100.0	373.9	217.8	—
Dimer	Byproduct	155.2	348.8	23.4	—
Trimer	Byproduct	256.8	439.9	15.9	—

^a Pasetti et al. (2014)

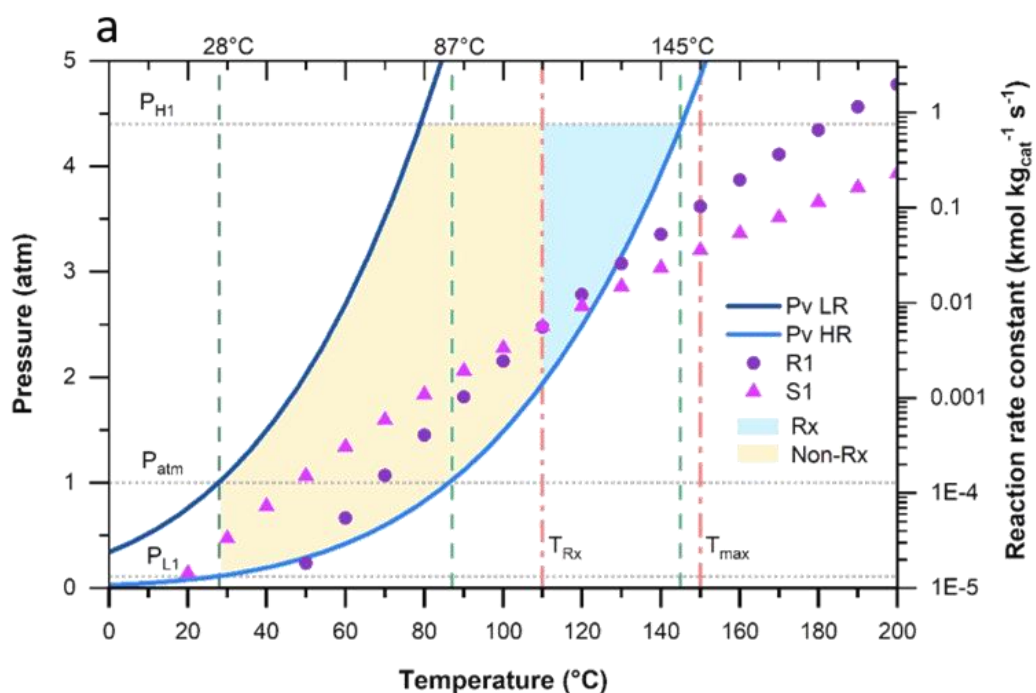


Figure 4.10. TAME case (Scenario 2): operating windows for single unit operation or rectification section (a) and stripping section (b)

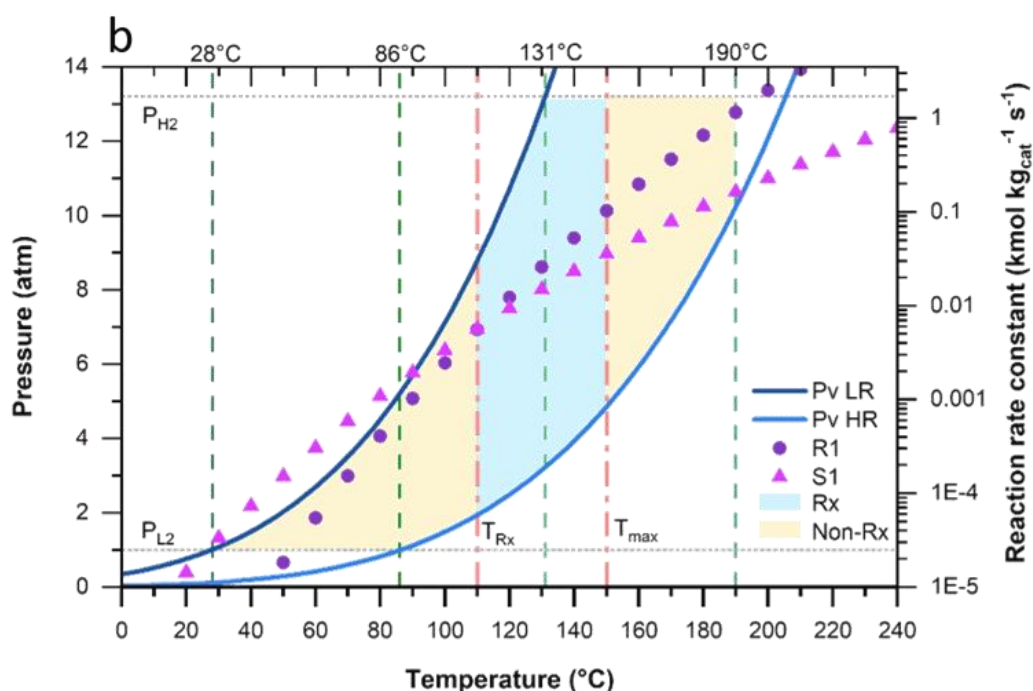


Figure 4.10. TAME case (Scenario 2): operating windows for single unit operation or rectification section (a) and stripping section (b) (Continued)

The operating bounds for the stripping and rectifying sections – pressures, condenser and reboiler temperatures – are the same for Scenarios 1 and 2, except that the temperature range for the reaction is reduced when side reactions are considered, as summarised in Table 4.9.

Table 4.9. Operating bounds for TAME production for Scenario 1 and Scenario 2

Parameter	Units	Stripping section	Rectifying section
Operating pressure	atm	0.11–4.4	1–13.2
Condenser temperature	°C	–	28–131
Reboiler temperature	°C	28 - 145	–
Maximum reaction temperature ^a	°C	150	150

^a Minimum reaction temperature for Scenario 2 is 110°C

4.4.4.3.4 Verifying operation bounds for the TAME system

This case study was devised to identify the effect of side reactions when constructing operating windows. Although the additional byproducts do not affect the assignment of LR and HR components, considering side reactions reduced the size of the window in which the reaction and separation can occur simultaneously. While the reaction could take place throughout the stripping section in Scenario 1, only temperatures above 110°C favour the main reaction over the side reaction in Scenario 2. In the rectifying section, the reaction could occur below 150°C in Scenario 1, but between 110 and 150°C in Scenario 2. This finding has important implications for process design practice, as these results demonstrate that the effect of side reactions could be identified from basic data used in operating windows.

Previous simulation studies for R-HIDiC (Pulido et al., 2011; Vanaki and Eslamloueyan, 2012; Gao et al., 2014) did not account for side reactions; hence results of Scenario 1 are used for comparison. Whereas the ranges of pressures for the stripping and rectifying sections contain the single values reported in the simulation studies, the location of the reactive section varies. Pulido et al. (2011) located the reactive section in the stripping section operating at 4 bar, while Vanaki and Eslamloueyan (2012) and Gao et al. (2014) located the reactive section in a rectifying section operating at 4 and 4.7 bar, respectively.

Although operation at 4 bar allows for stripping and rectifying sections to be entirely reactive in Scenario 1, when side reactions are considered, the range of temperatures where the reactive section can be placed is reduced. Regarding the use of operating windows for process synthesis, this means that the operating boundaries found could provide information on the constraints that reduce the design space. Studies investigating TAME production by RD reported operation at 4 bar (Subawalla and Fair, 1999; Klöcker et al., 2003). Operation in a single unit is possible, and reference values could be obtained from the high-pressure operating window in Figure (b), where three regions are evident: a rectifying section on the left-hand side, an integrated reaction and separation section in the middle, and the stripping section on the right-hand side. The range of operating pressures from 4.9 to 8.8 atm ensures the use of the largest reactive section within temperature limitations.

The findings of evaluating the same system under two scenarios have significant implications for understanding simplifying assumptions, whose effect could be already identified while constructing operating windows. In turn, this will allow strategies (e.g., alternative catalysts, additional kinetic experiments) to be incorporated to overcome certain limits of the operating window in preparation for detailed designs. Further simulation studies taking side reactions into account could assess their effect on the reaction window limits.

4.4.5 Challenges and opportunities

The fields of process synthesis, design and intensification are increasingly integrated through the development of hybrid methodologies using a range of input data and tools. Therefore, future challenges to advance the development and application of ARDT include the evaluation of new chemical systems and suitable metrics to evaluate performance.

The development of processes that involve new chemical and biochemical routes or catalysts can make the collection of physicochemical data difficult and expensive. Thus, the lack of data would make it difficult to apply the proposed methodology to new chemical systems or

processes that are under investigation. At the same time, this offers opportunities for the development of catalysts with better characteristics (catalytic, thermal, mechanical) and promotes the development of new analytical techniques and methods to aid the identification of basic thermodynamic properties and kinetics quickly and economically.

Due to the integration of functionalities, quantitative evaluation is challenging and covers different aspects such as productivity, economics, safety and environment. Therefore, metrics that compare new and conventional technologies are needed to fairly demonstrate the benefits and drawbacks of novel technologies.

4.4.6 Conclusions and future work

This work successfully demonstrated the use of expanding the boundaries of operating windows for reactive distillation by incorporating additional features (i.e., representative components, sliding windows) to help advance the application of advanced reactive distillation technologies in the early stages of process design, along with potential operating conditions that could be used to initialise design methods and rigorous simulations. The proposed two new concepts of representative components and a sliding window facilitate the representation of a complex multicomponent system while constructing the operating window. The proposed approach for constructing operating windows has shown that a range of operating conditions (e.g., condenser temperature, reboiler temperature, maximum reaction temperature and operating pressure) can be identified. Although the scope of this study was limited to an early-stage assessment, the findings of this research provide a starting point for further analysis of ARDT by providing initial values that could be used in various design methodologies and detailed simulations.

The proposed methodology to build the operating windows was effectively demonstrated in three case studies: methyl acetate production, lactic acid purification and TAME production. These case studies illustrate how complex features such as multicomponent feeds and side reactions can be represented in an operating window. For example, for methyl acetate production, it was found that the identified side reaction is not likely to occur at the operating conditions identified. In the case of lactic acid purification, a complex mixture of reactants, products, byproducts and intermediate products was successfully represented in an operating window even though no reliable data was available for one of the byproducts. One of the more significant findings for lactic acid production was that operation at vacuum conditions is needed, which provides guidance for selecting RD technologies. Finally, the effect of side

reactions was evidenced for TAME production. Considering side reactions reduced the size of the reaction window significantly, demonstrating that the impact of complex features could be identified at early stages.

The application of the proposed approach in three case studies has shown that operating boundaries could be identified using basic data in the early stages of process design, which is verified by the results of detailed simulation studies from the literature. The findings of this work provide well-supported values for the operating regions, which could be used as a starting point for further evaluation with more detailed simulations and design methods. The insights gained from this study may be of assistance to process designers who are screening the design space, and the results of the operating windows assessment could help to systematically plan subsequent steps with confidence. In spite of some limitations, this study contributes to understanding the factors affecting operating bounds, especially when considering side reactions and temperature restrictions (e.g., degradation) that are typically overseen or simplified during process synthesis.

The approach proposed here will be complementary to a ruled-based methodology that will incorporate additional characteristics of the system, such as the rates of reaction (e.g., relatively fast or slow) and the impact of azeotropes to evaluate advanced reactive distillation technologies systematically during process synthesis.

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4.5 Supplementary Information for Publication 3

4.5.1 Introduction

The degree of integration of functionalities based on the overlap between the reaction and separation windows is presented graphically in Figure S4.11.

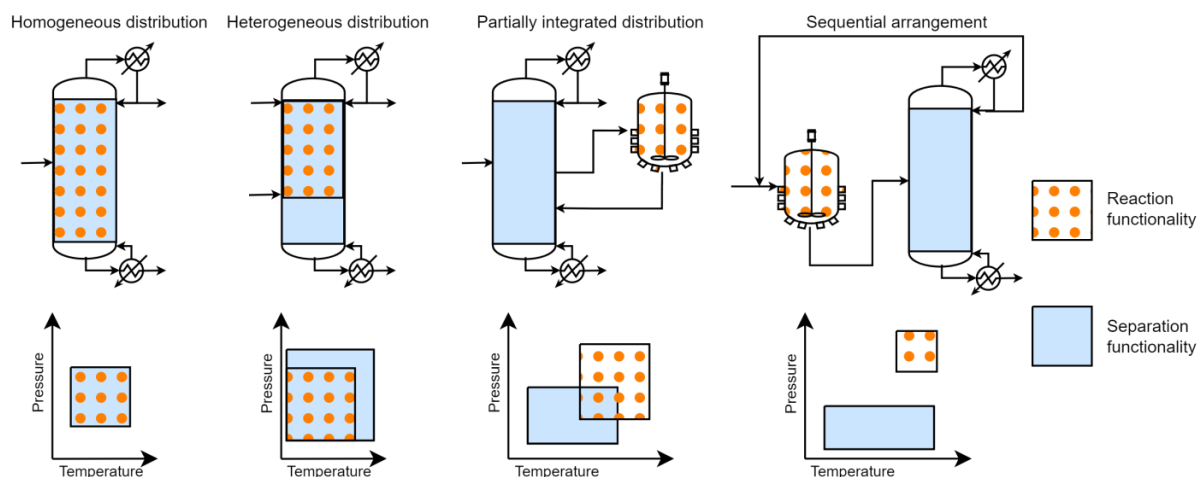


Figure S4.11. Representation of different levels of integration (Adapted from Tylko et al. (2006))

4.5.2 Sliding window

Figure S4.12 provides a graphical representation of the concept of a sliding window and the operating points that could be identified.

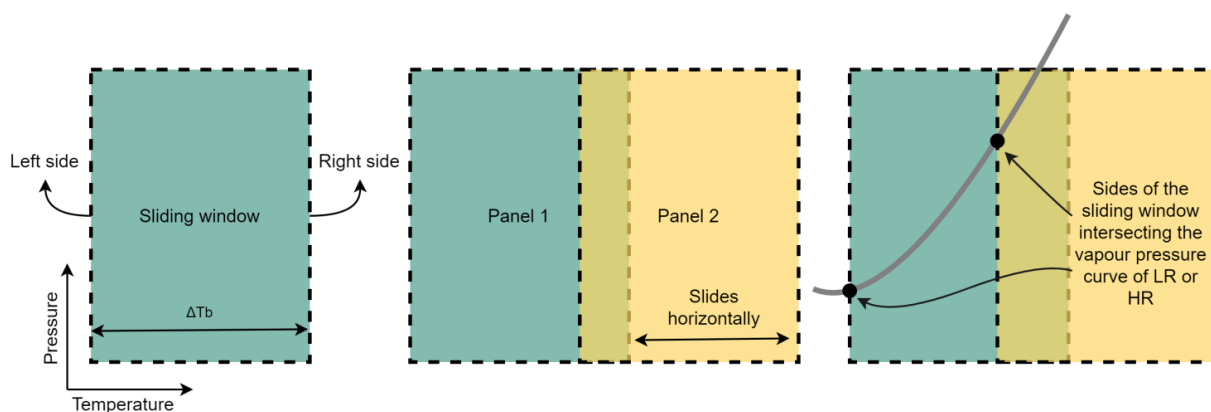


Figure S4.12. Concept of a sliding window

4.5.3 Methodology for building operating windows

4.5.3.1 Systematic guide for constructing the operating window

This section provides a graphic explanation in Figure S4.13 about the sequence for constructing the operating window and how the data is used. Finally, the outcomes of each step are also identified.

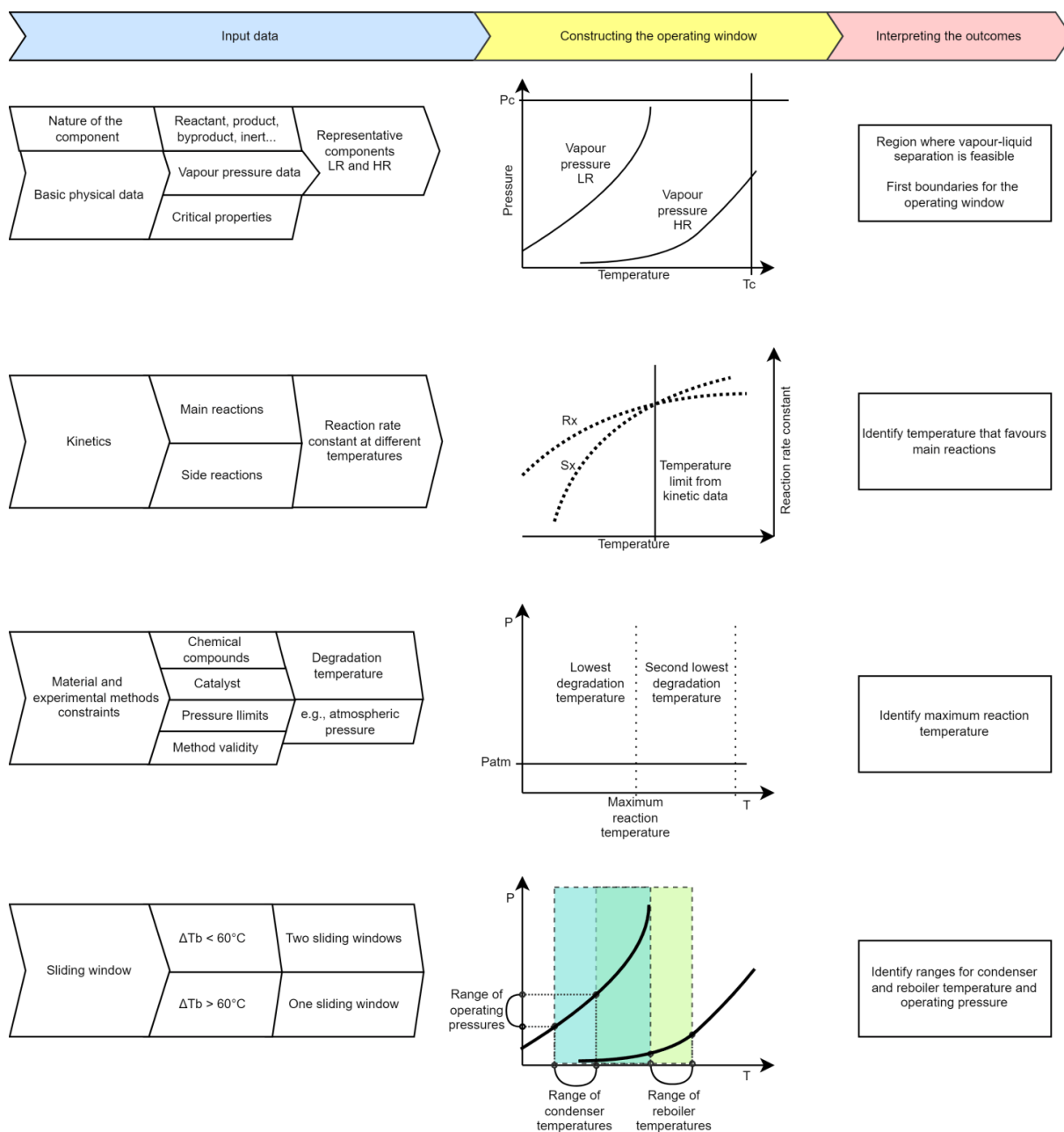


Figure S4.13. Graphical overview for the construction of operating windows

4.5.3.2 Locating the panels of the sliding window

Assuming a minimum temperature approach of 20°C , the left side of the sliding window starts at 40°C and then moves horizontally until 60°C , which sets a limit for the condenser temperature. The intersections of the left sides of each panel of the sliding window and the vapour pressure curve of the light representative component help identify a range of suitable operating pressures, which are read in the primary vertical axis. These values are for reference only, as lower temperatures via refrigeration could be used to avoid thermal degradation. Higher temperatures may be employed to promote a reaction while avoiding thermal degradation.

If the degradation temperature limit is still far to the right side of the sliding window, the reaction could be accelerated by using higher temperatures. If evaluating multiple reactions, a vertical temperature limit indicates a threshold where one reaction could be enhanced over the other. Therefore, the sliding window travels along the temperature axis until the right side reaches a temperature constraint imposed by thermal degradation or utilities. Typical steam levels or degradation temperatures primarily define reboiler temperatures. A graphical explanation to locate the sliding window is detailed in Figure S4.14.

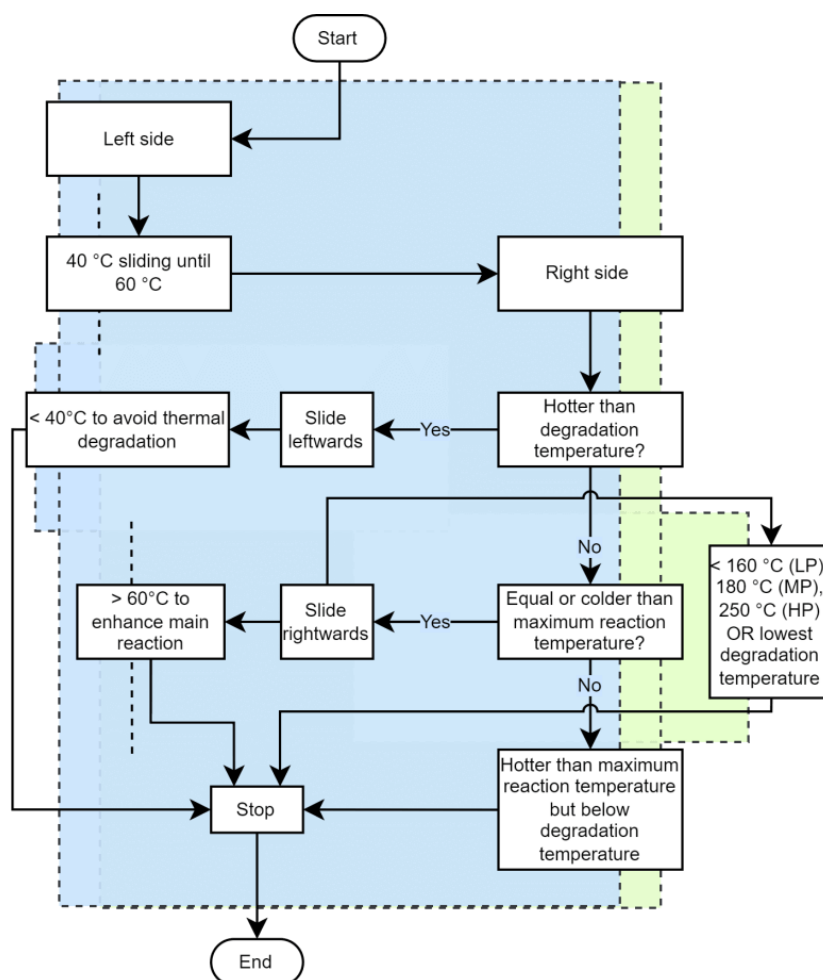


Figure S4.14. Flowchart to locate the sliding window for systems with ΔT_b larger than 60°C

For systems featuring a ΔT_b lower than 60°C, R-HIDiC can take advantage of operation at different pressures, hence the need for two sliding windows. Using reference temperatures based on utilities is not relevant because an ideal R-HIDiC can satisfy the cooling and heating needs within the configuration. However, supplementary heating and cooling – especially for starting up – are often provided by a trim-condenser and trim-reboiler, respectively, in a partial R-HIDiC configuration (Shahandeh et al., 2014). For this reason, a reference pressure is used to locate the first sliding window.

First, the low-pressure section containing the heaviest compounds – and potentially a trim-reboiler – corresponds to the stripping section. The right side of the sliding window is located at the intersection between the vapour pressure curve of the heavy representative component and atmospheric pressure. Subsequently, the left side of the window ends one ΔT_b away to the left. Then, the second panel of the sliding window moves rightwards and stops one ΔT_b away from where it started. The sides located one ΔT_b away towards the cold and hot ends intersect with the vapour pressure curve of the heavy representative component to find a range of operating pressure for the stripping section and the temperatures in the bottom – or for the trim-reboiler.

The high-pressure section contains the lightest compounds – and potentially a trim-condenser – and corresponds to the rectifying section, whose operating window is located with a second sliding window. The pressure bounds found for the stripping section are multiplied by 1.3 and 3 (reference compression ratios) to find a suitable range of operating pressures. If the low-pressure limit multiplied by the compression ratio gives values below atmospheric, it is suggested to start the analysis by locating the left side of the sliding window at the intersection between the vapour pressure curve of the light representative component and atmospheric pressure. In the same manner, the high-pressure limit multiplied by the compression ratio indicates the location of the second panel of the sliding window. The intersections of the left sides indicate the top temperatures – or the trim-condenser temperature if needed. Guidance for the location of the two sliding windows to locate the stripping and rectifying section is detailed in Figure S4.15.



Figure S4.15. Flowchart to locate the sliding windows for systems with ΔT_b lower than 60°C

4.5.4 Datasets for case studies

4.5.4.1 Case 1: Production of methyl acetate

Datapoints used to represent the esterification of acetic acid correspond to a pseudo-homogeneous model using activities by UNIQUAC from the work of Pöpkén et al. (2000), who used Amberlyst 15 between 303.15 and 343.15 K.

Table S4.10. Kinetic parameters for the reactions in the methyl acetate system

Reaction	Pre-exponential factor (kmol/kg s)	Activation energy (kJ/kmol)	Reference
Esterification of acetic acid	2.96E+04	49190	(Pöpkén et al., 2000)
Dehydration of methanol	1.95E+08	133800	(Lei et al., 2011)

Datapoints for the dehydration of methanol were calculated from the work of Lei et al. (2011), who used Amberlyst 35. Original kinetic parameters were presented on a volume basis instead of a molar basis. Therefore, the density of the liquid phase was calculated at standard conditions assuming molar fractions of 0.2 for DME, 0.4 for water and 0.4 for methanol to obtain units of kmol/kg s.

4.5.4.2 Case 2: Purification of lactic acid

Table S4.11. Kinetic parameters for the reactions in the lactic acid system

Reaction	Pre-exponential factor (kmol/kg s)	Activation energy (kJ/kmol)	Reference
Esterification of lactic acid	2.17E+04	48733	(Sanz et al., 2004)
Esterification of succinic acid	1.10E+07	72855	(Dudáš et al., 2014)
Esterification of monomethyl succinate	4.40E+07	78646	(Dudáš et al., 2014)
Oligomerisation of lactic acid	2.00E+01	52000	(Asthana et al., 2006)
Oligomerisation of dilactic acid	5.70E+00	50800	(Asthana et al., 2006)

4.5.4.3 Case 3: Production of tert-amyl methyl ether

Table S4.12. Kinetic parameters for the reactions in the TAME system

Reaction	Pre-exponential factor (kmol/kg s)	Activation energy (kJ/kmol)	Reference
TAME production from 2M1B	1.33E+08	76104	(Luyben and Yu, 2008)
TAME production from 2M2B	1.37E+11	98230	(Luyben and Yu, 2008)
Isomerisation of isoamylenes	2.72E+10	96523	(Luyben and Yu, 2008)
Dimerisation to 2,3,4,4-tetramethyl-1-hexene	5.61E+03	50423	(Cruz et al., 2007)
Trimerisation to 2,4,6,6,7,7-hexamethylnon-3-ene	1.61E+06	62025	(Cruz et al., 2007)
Dehydration of methanol	1.95E+08	133800	(Lei et al., 2011)

4.5.5 Analysis of the methyl acetate system: Exploring opportunities for internal heat integration

As the temperature difference between the light and heavy representative components is slightly above 60°C, the potential application of R-HIDiC was evaluated using two sliding windows. First, the low-pressure section is located using a reference pressure of 1 atm at the intersection with the HR vapour pressure curve on the right side of the sliding window. The low-pressure limit is read on the intersection with the left side of the sliding window. Then, the window slides one ΔT_b away to the right to locate the high-pressure limit. Low- and high-pressure limits correspond to 0.1 and 4.94 atm. Temperature bounds for the bottom section – or trim-reboiler – containing the heaviest compounds of the system are 57 and 179°C (Figure S4.16, a).

When evaluating the second sliding window, atmospheric pressure is used as the low-pressure limit for the rectifying section because the low-pressure limit found for the stripping section is below atmospheric. The high-pressure limit corresponds to 14.82 atm. As a result, the top temperature bounds for the rectifying section – or trim-condenser – are 56 to 154°C.

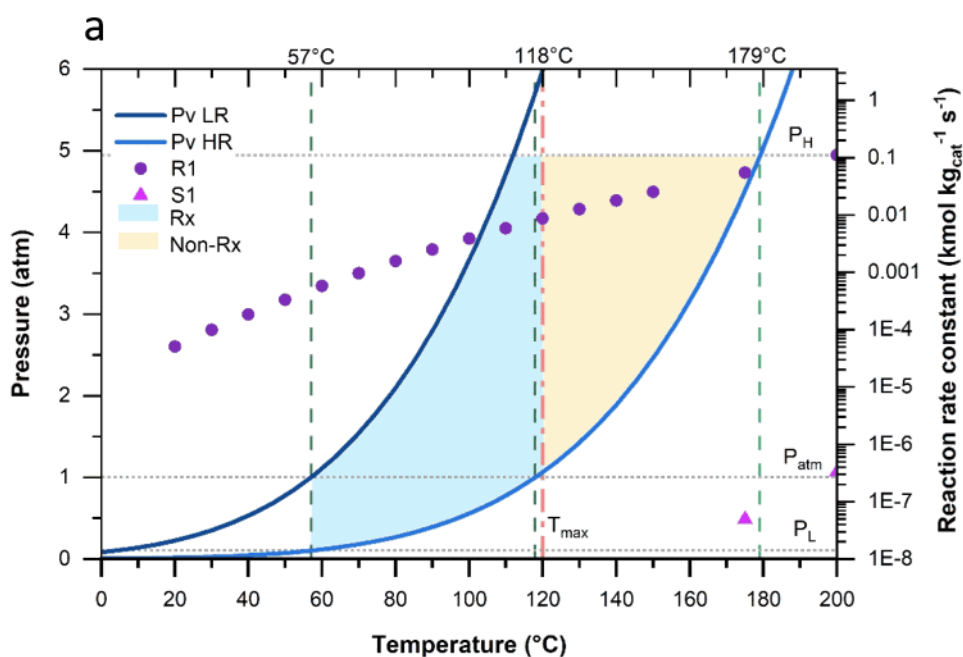


Figure S4.16. Methyl acetate case: operating windows for the low-pressure stripping section (a) and high-pressure rectifying section (b) (Pv LR: vapour pressure of the light representative component, Pv HR: vapour pressure of the heavy representative component, R1: reaction rate constant for main reaction, S1: reaction rate constant for side reaction, Rx: reactive zone, non-Rx: non-reactive zone, PH: high-pressure boundary, PL: low-pressure boundary, Tmax: maximum reaction temperature, TdAA: degradation temperature of acetic acid)

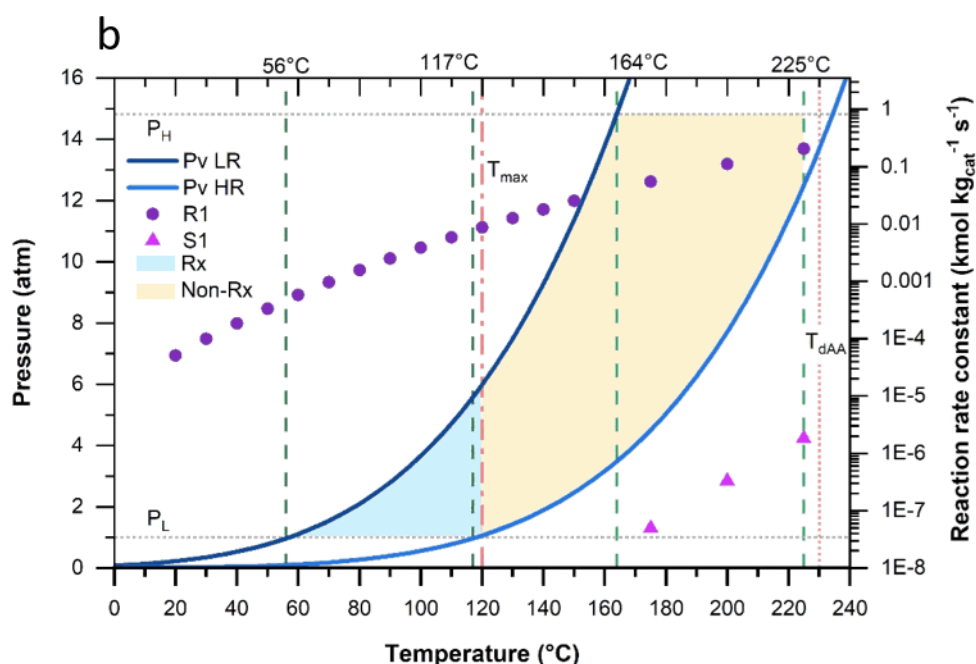


Figure S4.16. Methyl acetate case: operating windows for the low-pressure stripping section (a) and high-pressure rectifying section (b) (Pv LR: vapour pressure of the light representative component, Pv HR: vapour pressure of the heavy representative component, R1: reaction rate constant for main reaction, S1: reaction rate constant for side reaction, Rx: reactive zone, non-Rx: non-reactive zone, PH: high-pressure boundary, PL: low-pressure boundary, Tmax: maximum reaction temperature, TdAA: degradation temperature of acetic acid) (Continued)

The location of the reactive section depends only on the maximum reaction temperature (120°C). Therefore, the reactive section can be accommodated in either section when using two separate sections. However, the rectifying section at low pressure presents a slightly larger window where the reaction and separation can occur simultaneously. The operating conditions identified for a potential operation in an R-HiDiC are summarised in Table S4.13.

Table S4.13. Operating bounds for the production of methyl acetate

Parameter	Units	Stripping section	Rectifying section
Nominal pressure	atm	0.1–4.94	1–14.82
Condenser temperature	°C	–	56–154
Reboiler temperature	°C	57–179	–
Maximum reaction temperature	°C	120	120

When using these values as a reference to initialise a detailed simulation, the range of values tested narrows. For example, if the stripping section is initialised with an operating pressure of 1 atm, the rectifying section pressures will vary between 1.3 and 3 atm.

Although hydrolysis of methyl acetate was not evaluated, and since the components participating in the system are the same, the results obtained from evaluating the operating windows for two separate sections are compared with those available for hydrolysis of methyl

acetate in R-HIDiC. Lee et al. (2010) optimised an R-HIDiC configuration and found that low- and high-pressure sections operate at 1 atm and 4.5 atm, respectively. Li et al. (2015) worked in a narrower range with a low-pressure section at 1.1 atm and a high-pressure section at 3.6 atm. Finally, the study of Chen et al. (2020) demonstrated that pressure increase in the reactive section from 3.1 atm to 3.9 atm benefits the rate of reaction, which cannot be observed in Figure S4.16 as the reaction rate constant for the hydrolysis of methyl acetate is not presented. Operation at high pressure for methyl acetate hydrolysis is likely to maintain the main reactant in the liquid phase, given that it is the most volatile substance in the system. Together these results provide important insights for technology evaluation, particularly by providing potential operating conditions values, which were compared with those available in the literature.

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Chapter 5

A systematic methodology for the synthesis of advanced reactive distillation technologies

5.1 Preface to Publication 4

The lack of synthesis and design methodologies that account for advanced reactive distillation technologies motivated the development of a systematic methodology focusing on R-DWC, R-HiGee, CCD, R-HIDiC, and MA-RD presented in Chapter 5 with Publication 4 and its Supplementary Information, the final output of this research.

Publication 4 addresses Objective 5 of this PhD thesis:

5. To establish a synthesis methodology that uses first principles and heuristics to qualitatively the advantages and disadvantages of advanced reactive distillation technologies applied to a chemical system to provide insights for the development of basic process flowsheets and to verify the validity of the results with industrially relevant case studies

Publication 4 proposes a systematic methodology to enable a quick and early-stage assessment of the technical feasibility of advanced reactive distillation technologies using first principles and heuristics. The methodology guides the selection of technologies by providing high-level questions grouped into four categories that allow a progressive evaluation of the system using basic thermodynamic properties and kinetic parameters. The four criteria are:

1. Composition and splits
2. Basic properties and operating windows
3. Kinetics
4. Phase equilibria

The synthesis methodology is applied and analysed in five case studies. Each case presents different complexities, for example, the effect of side reactions, the need for forward and

reverse reactions, and incomplete information regarding the chemical system. The methodology offers flexibility to assess the effect of these complexities by proposing different scenarios, which depend on the information available and the practitioner's judgment that defines the design problem. The five case studies evaluated are:

- Purification of lactic acid
- Production of dimethyl ether
- Production of tert-amyl methyl ether
- Production of methyl acetate
- Production of cyclohexane

The methodology outcomes provide a qualitative indication of the technical feasibility and potential benefits of each technology and novel process flowsheets to satisfy the design problem. The results are verified with simulation and conceptual design studies from the research literature. The methodology aims to motivate process designers to consider advanced reactive distillation technologies by providing a structured workflow to reduce the design space and guide the selection of technologies using data that can be gathered from open sources with less computational effort than mathematical programming approaches.

5.2 Publication 4

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A systematic methodology for the synthesis of advanced reactive distillation technologies

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Abstract

This study is the first to provide a systematic approach to assessing the potential of advanced reactive distillation technologies to expand the applicability of reactive distillation. The work presented here focuses on the synthesis of advanced reactive distillation technologies, proposing a conceptually based methodology for early-stage screening. The methodology uses basic thermodynamic and kinetic data to navigate a decision-making flowchart in four steps: compositions and splits, basic properties and operating windows, kinetics and phase equilibria. The results qualify advanced reactive distillation technologies as advantageous, technically feasible or not applicable. Five industrially relevant case studies illustrate the application of the methodology to develop preliminary process flowsheets. The proposed methodology aims to guide technology selection using basic data, while providing flexibility to meet the objectives of the design problem. This methodology contributes to integrating a technology-oriented approach normally followed in process intensification studies into a process systems engineering approach by developing a conceptual flowsheet in the early stages of process design.

Keywords: process intensification, reactive distillation, synthesis methodology, process systems engineering

5.2.1 Introduction

Traditional approaches for chemical process synthesis and design typically rely on the use of conventional unit operations that perform a single task. This inherent limitation results in configurations containing numerous units and recycle streams. Consequently, processes become complex and costly, often facing difficulties in meeting current and future challenges for the chemical and biochemical industries. Therefore, the process development community requires novel approaches, especially in the early stages when numerous processing options need to be rapidly evaluated with limited data.

Process intensification (PI) adds a disruptive shift towards innovative technologies by addressing the phenomena at various stages without confining the alternatives to the classical 'unit operation' concept (Van Gerven and Stankiewicz, 2009). Synergy – one of the PI domains – exploits the interactions of combining two or more functions in a single processing step, such as reaction and separation in reactive distillation (RD). A synergistic effect occurs when the reaction improves separation by overcoming azeotropes, while the separation improves reaction by increasing reaction rates, overcoming chemical equilibrium, and improving selectivity (Kiss, 2017). Other benefits of RD include capital and operating cost savings, reduced plant footprint, and better environmental performance when compared to a conventional reactor-distillation sequence (Sundmacher and Kienle, 2003). However, RD requires that the reaction and separation operating conditions overlap, which restricts its wider use (Kiss et al., 2019). Advanced reactive distillation technologies (ARDT) integrate the benefits of RD and additional PI features, which can enlarge the range of potential operating conditions, enabling a larger overlap between reaction and separation while decreasing the number of units due to the integrated functions (Pazmiño-Mayorga et al., 2023). The ARDT in scope are reactive dividing-wall column (R-DWC), catalytic cyclic distillation (CCD), reactive internally heat-integrated distillation (R-HiDiC), reactive high-gravity distillation (R-HiGee), and membrane-assisted reactive distillation (MA-RD).

This work proposes a conceptually based systematic approach for early screening of ARDT. This approach aims to guide the selection of feasible technologies during the development of flowsheets to address the design problem for a specified chemical system. Challenges for the application of ARDT are discussed in the problem statement section. Then, the main features and insights for process synthesis for R-DWC, CCD, R-HiDiC, R-HiGee, and MA-RD are described. The research approach includes the development, scope, structure and application

of the methodology, including interpretation of results. Finally, five case studies demonstrate the application of the methodology to identify potential configurations, and the results of rigorous simulations available in the literature serve to confirm their feasibility.

5.2.2 Problem statement

Industrial applications of ARDT are extremely scarce. Although conventional RD is established for equilibrium-limited reaction systems (Luyben, 2013; Skiborowski, 2018), the lack of robust methods and tools for process design and simulation and pilot and industrial tests limit the uptake of ARDT (Kiss et al., 2019). Synthesis methods that result in a conceptual flowsheet, following a process systems engineering approach, are also lacking (Keil, 2018). Methods for evaluating the feasibility of RD in a given context are limited to standalone units (Doherty and Malone, 2001; Shah et al., 2012; Muthia et al., 2018) or reactive-separation systems, including conventional and intensified units (Holtbruegge et al., 2014a; Garg et al., 2020). However, synthesis and design of processes that apply ARDT have hardly been explored. In this work, the research question relates to whether a structured flowchart can be developed to identify which, if any, ARDT are best suited to exploit a given chemical reaction to produce a desired product.

Previous studies to develop reaction or reaction–separation processes on a laboratory scale or through simulation tend to oversimplify complex features that can potentially affect operation. These features include impurities that interact with other species, dilute feeds, constraints for materials of construction and the thermal and chemical stability of the participating components, undesired side reactions and azeotropes. However, by generalizing features of the operation and equipment, the methods and results of earlier studies can highlight decision points and relevant characteristics of the process system that could guide the selection of technologies.

This study proposes a systematic conceptually-based methodology for the initial evaluation of ARDT during flowsheet development. The methodology uses basic thermodynamic and kinetic properties, applying first principles and heuristics to qualitatively assess the application of ARDT. Overall, it aims to enable informed decisions prior to detailed process design.

5.2.3 Advanced reactive distillation technologies: Main features and insights for process synthesis

5.2.3.1 Reactive dividing wall column (R-DWC)

Reactive dividing wall column combines already intensified technologies: dividing wall column and reactive distillation in a single vessel (Weinfeld et al., 2018). Figure 5.1 (a) illustrates the concept of an R-DWC containing one reactive section in the feed side and a dividing wall located in the middle. Other arrangements concerning the location and number of feed streams, dividing walls and reactive sections are possible (Mueller and Kenig, 2007; Weinfeld et al., 2018). R-DWC allows at least three outlet streams, facilitating removal of intermediate-boiling components and recycling of reactants both internally (via reflux and boilup) and externally in the draw stream when conversion is incomplete. The dividing wall and side stream(s) change the composition profiles within the column, compared to a conventional RD column. Therefore, a reaction could be promoted or prevented because of the change in composition at that stage relative to RD. This is relevant when undesired parallel reactions reduce selectivity towards the main product. R-DWC can operate under vacuum, at and above atmospheric pressure (Kaibel, 2014), allowing for a wide range of conditions that could favour reactions in the liquid phase, although operation at a single pressure can limit the application of R-DWC. Technology readiness based on pilot and industrial experience is intermediate (Kiss et al., 2019).

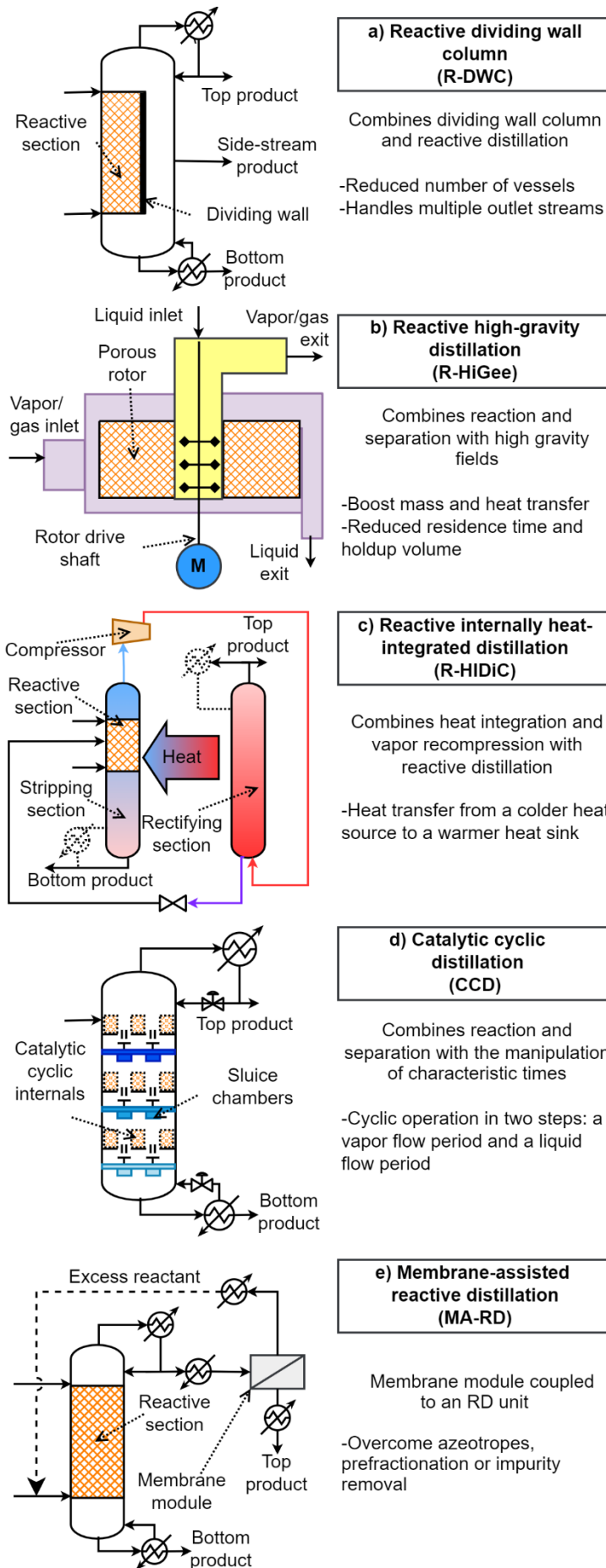


Figure 5.1. Main features of five advanced reactive distillation technologies

5.2.3.2 Reactive high-gravity distillation (R-HiGee)

Reactive high-gravity distillation combines intensified gravitational force to enhance mass, heat and momentum transfer to favour phase separation and reaction (Figure 5.1 (b)) (Cortes Garcia et al., 2017). Consequently, required residence time and holdup volumes are reduced, resulting in smaller equipment. Rotating packed beds have been identified as a suitable HiGee contactor to perform RD (Cortes Garcia et al., 2017; Kiss et al., 2019; Neumann et al., 2018). This technology is particularly suitable for diffusion-limited systems (e.g., high viscosity) and when the reaction network includes series reactions, where desired products could be transformed into unwanted byproducts (Quaderer et al., 2000). Therefore, a narrow residence time distribution helps to achieve high selectivity to the desired product. The features of chemical systems that are suited to R-HiGee are diffusion-limited liquids, and fast reactions with secondary reactions in series. Rotating packed beds can be advantageous for high-pressure operation (Sudhoff, 2022b) and vacuum distillation (W. Li et al., 2017). Despite an industrial application of a rotating packed bed (RBP) for the production of hypochlorous acid has reached a high technology readiness level, R-HiGee is not yet considered a mature technology (Neumann et al., 2018).

5.2.3.3 Reactive heat-integrated distillation column (R-HiDiC)

Reactive heat-integrated distillation columns (R-HiDiC) combine the benefits of reactive distillation and internally heat-integrated distillation columns by applying vapour recompression and heat integration. The stripping section, operating at a lower pressure, acts as a heat sink. Vapour exiting the stripping section is pressurised with a compressor, and then enters the rectifying section that acts as a heat source, schematically represented in Figure 5.1 (c). Using different pressures in the column sections could potentially increase the range of operating conditions compared to RD (Kiss and Olujić, 2014). From a practical point of view, equipment realisation is challenging, and the literature about non-reactive HiDiC presents various design alternatives (Kiss and Olujić, 2014). In a configuration that has been successfully applied industrially, SuperHiDiC, the heat exchange is realised in a limited number of side heat exchangers, where the stages are not necessarily at the same elevation (Wakabayashi and Hasebe, 2015). In non-reactive HiDiC, the pressure ratio between the stripping and rectifying sections can vary between 1.3 and 3 to avoid a costly compression task (Kiss and Olujić, 2014; Suphanit, 2010). As a rule of thumb, the temperature difference between the lightest and the heaviest compounds (ΔT_b) should not exceed 60°C (Kiss, 2013). Thus, the feasibility of R-HiDiC

is evaluated using boiling points at different pressures while considering a suitable compression ratio.

5.2.3.4 Catalytic cyclic distillation (CCD)

Catalytic cyclic distillation (CCD) exploits the synergies of combined reaction and separation by manipulating characteristic times in a cyclic operation. The two-step cycle consists of a vapour-flow period where vapour travels upwards while the reaction occurs in the liquid phase and a liquid-flow period where the liquid flows downwards from one tray to the next, avoiding remixing (Figure 5.1 (d)) (Pătruț et al., 2014). The residence time can be enlarged by manipulating the duration of the vapour flow period. Therefore, CCD is especially suited for systems featuring reactions with an intermediate to slow reaction rate, but not too slow that it is better to use a conventional reactor-separator sequence. As a result, CCD may be indicated if the reaction rate is intermediate to slow. Unique internals suited for cyclic operation are not suitable for vacuum operation (Kiss and Maleta, 2018). Technology readiness based on pilot and industrial experience is low (Kiss et al., 2019).

5.2.3.5 Membrane-assisted reactive distillation (MA-RD)

A membrane module coupled to an RD column helps overcome thermodynamic limitations by introducing a separation mechanism based on the difference in chemical potential using partial pressures. Membrane separation methods that can complement separations by distillation are pervaporation or vapour permeation (Holtbrügge, 2016; Lutze and Gorak, 2013). The membrane module can be located on an inlet stream to selectively remove impurities or prefractionate the mixture, or on an outlet stream to break azeotropes or recover homogeneous catalysts, where the latter typically applies nanofiltration (Figure 5.1 (e)) (Lutze and Gorak, 2013). In this methodology, MA-RD is suggested when a problematic azeotrope is present at a similar temperature to those of the components to be separated and obtained as an outlet stream. Operating pressures above atmospheric are preferred for the reactive distillation column because the flow across the membrane is driven by the pressure drop, so a stream at sub-atmospheric pressure entering the membrane module may lead to engineering challenges.

5.2.4 Research approach

5.2.4.1 Development of the synthesis methodology

This work used data and results (e.g., feed and product specifications, type of reactions and kinetics models, type of catalyst, operating conditions) from reports, patents and published studies focusing on a specific technology. These studies cover diverse scopes (e.g., technical, economic, environmental), which were used as a basis for identifying which characteristics favour the use of a particular technology. The secondary research data and results were organised and compared to find commonalities that could aid flowsheet development, where technical feasibility is an essential preliminary checkpoint for further design. High-level questions based on thermodynamic and kinetics parameters were formulated in a conceptual framework (Pazmiño-Mayorga et al., 2022a). In this work, these high-level questions are organised systematically in a decision-making flowchart to identify the characteristics that distinguish the advantages and disadvantages of different ARDT following a knowledge-based approach based on first principles, heuristics, and process intensification principles (Pazmiño-Mayorga et al., 2022b).

5.2.4.2 Scope of the synthesis methodology

This work focuses on a subset of the design problem for rapid evaluation of ARDTs (i.e., R-DWC, R-HiGee, R-HiDiC, MA-RD and CCD). The methodology covers equilibrium-limited reactions in the liquid phase, heterogeneously catalysed, as is typically the case in RD processes (Tylko et al., 2006). Application of the synthesis methodology to homogeneously catalysed reactions should be done with caution. This is because homogeneous catalysts tend to be more active than heterogeneous catalysts, so different ranges of reaction rates could apply. Additionally, it should be ensured that the homogeneous catalyst is sufficiently available within the liquid phase, and this could be included when evaluating operating windows. A special case applied to fluid separations is the introduction of a ‘reactive separation agent’ (RSA) (analogous to a mass separation agent used to facilitate separations) that promotes a reversible reaction, where the forward and reverse reactions are needed to achieve the desired separation. With an appropriate RSA, the products from the forward reaction can be easily separated, and the reverse reaction is finally used to recover the original target component. In addition, fast solid-catalysed reactions of a stripping gas absorbed in the liquid phase could be explored for suitability where rapid removal of reaction products is needed (Cortes Garcia et al., 2017).

This general methodology accounts for features relevant to large-scale industrial applications. These features include azeotropes, impurities, multicomponent mixtures, difficult separations and types of utilities, while laboratory-scale investigations and simulation-based studies often do not consider them.

This methodology is proposed for the early stages of process design when information about the chemical system is often limited. However, complex feeds, such as biomass-derived oils for biodiesel production that have highly variable compositions and are difficult to characterise, are out of scope. While a model compound could be used to represent the feed, results are expected to depend significantly on which model compound is selected as well as the availability of data (Albuquerque et al., 2021; Kiss et al., 2012). In addition, complex reaction networks that increase the number of interdependent interactions cannot be assessed in the methodology, as identified for the production of iso-octane where two main reactions (dimerisation and hydrogenation) compete with the formation of various oligomers of isobutene (Díaz Velázquez et al., 2020; Goortani et al., 2015; Talwalkar et al., 2006). Nor does this synthesis approach account for possible miscibility gaps because of their sensitivity to composition and operating conditions. Given the exploratory nature of the proposed methodology, capital costs and opportunities for heat integration are not investigated, being outside the scope. However, efficient use of energy is partially addressed when evaluating operating windows.

5.2.4.3 Decision-making flowchart

The methodology is organised into four steps that group different aspects of the chemical system assessed: 1) compositions and splits, 2) basic properties and operating windows, 3) kinetics and 4) phase equilibrium. Each step contains one or more high-level questions denoted as the ‘starting question’ that invites the user to collect information about the chemical system to identify potential interactions and their effects. These ‘starting questions’ were organised systematically, maintaining a balance between the depth and breadth of chemical system features to facilitate analysis and focus on those features that could significantly affect flowsheet development. This is important when realistic features that increase the complexity of the problem are included.

The ‘decision points’ refine the queries posed by the high-level questions to distinguish between interactions that may (or may not) affect the operation. Potential decisions include: options for the selection of technologies, yes/no answers, or ranges of values. Figure 5.2

shows the colour code used to denote the sequence of actions aiding decision-making and the results of the methodology.

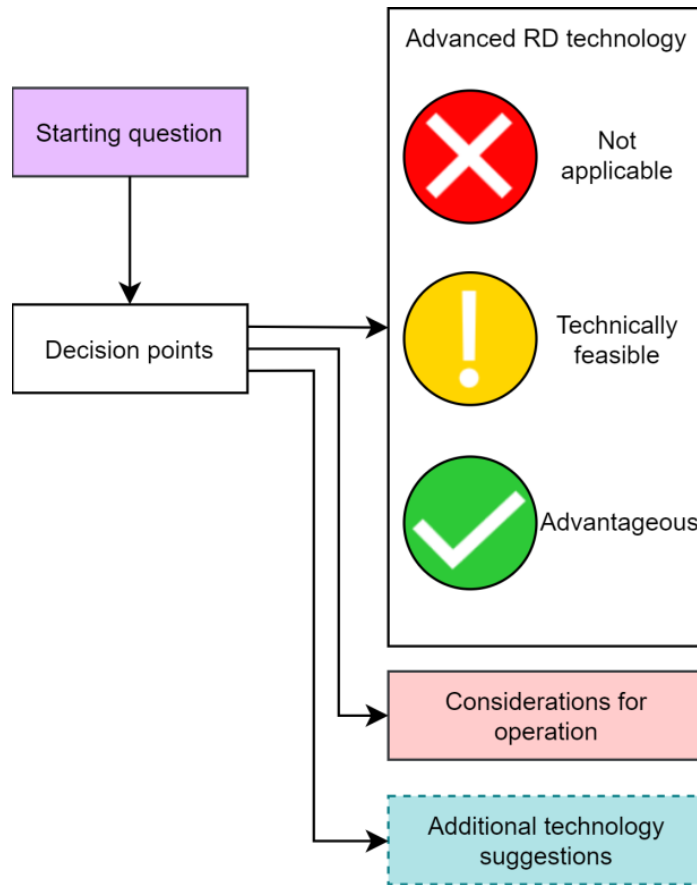


Figure 5.2. Colour code used in the decision-making flowchart

- Options for the selection of technologies are presented with a traffic light system. Green indicates the technology is advantageous, amber indicates it is technically feasible with no particular advantage, and red eliminates a technology due to hardware or operating specifications limitations. Additional units that could be explored beyond the scope of the methodology are presented in dashed line blocks. Actions that can be solved within the scope of the methodology when evaluating another starting question are presented with a solid line block.
- Yes/no answers can lead to another decision point, a range of values, or a particular technology. In some cases, both yes and no answers may be valid – for example when a feasible range of operating pressures spans both above and below atmospheric pressure. In these cases, two different paths may be followed in the flowchart.
- Ranges of values are used for reference only and do not represent a hard limit. These values can fluctuate depending on the system and operating conditions, so more than one option can be selected.

5.2.4.3.1 Step 1: Compositions and splits

Identifying components and compositions, particularly for the feed and main product, is essential to define the design problem. Components can include reactants, products, byproducts, catalysts and impurities.

- Reactants and products are target components of the operation as they are involved in the main reaction.
- Byproducts result from parallel or series reactions, which are usually non-desired because they consume valuable raw materials and complicate downstream processing.
- Impurities accompanying the main reactants are evaluated based on their quantity and their chemical interactions (whether reactive or inert) to identify potential effects on process performance. Reactive impurities could add or remove energy due to the heat of reaction, and inert impurities in large amounts increase the material recycle in the system. This evaluation is important as, from the beginning, it is possible to identify potential increase in costs due to changes in energy use and large equipment (Sinnott and Towler, 2020; Smith, 2016).

A special case for a feed is when it is an intermediate process stream that contains a large number of components. Listing all the impurities and choosing only those representing a light inert, heavy inert, or potentially reactive compound can help characterise their impact while facilitating analysis. Different scenarios can be established (stoichiometric vs excess reactant, partial vs complete conversion, series reactions, and byproduct formation) to identify potential impacts. Figure 5.3 presents the decision-making flowchart to evaluate compositions and splits.

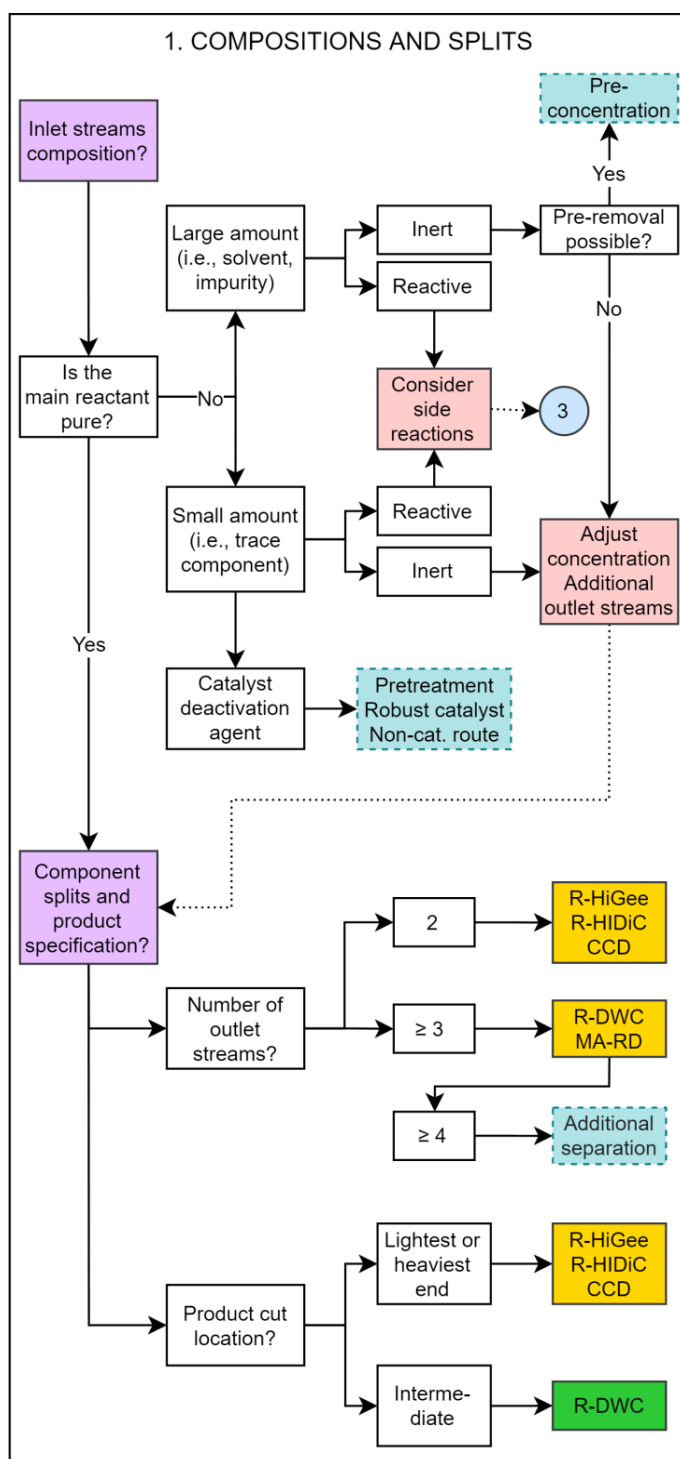


Figure 5.3. Step one: compositions and splits flowchart

Inlet streams' compositions

The feed stream composition considers 1) the main reactant and 2) 'other components' that are in large quantities or that may interact with critical reactants or solid catalysts. Relevant interactions may arise when an inert component is present in significant amounts, when a reactive component induces side reactions, or when a component can deactivate a solid catalyst. The decision-making procedure uses these interactions to suggest actions or other decision stages in the methodology. An explanation of these actions is provided hereafter:

- Inert: These could be removed in a pre-concentration stage when present in large amounts. However, inert compounds concentrations can sometimes be adjusted to favour conversion, selectivity and yield. For example, on the one hand, more inert material is advantageous to achieve a dilution effect that suppresses reaction rates and dampens the effect of the heat of reaction. Conversely, a lower inert concentration can reduce byproduct formation by shifting the equilibrium away from the undesired byproduct from side reactions (Sinnott and Towler, 2020; Smith, 2016). Finally, inert compounds need to be considered when defining the output streams for their removal.
- Reactive: When the component promotes side reactions that can impact yield, selectivity, and operating costs. Side reactions are considered when evaluating kinetics.
- Catalyst deactivation agent: Whether the deactivation is temporary or permanent, the feed could be pre-treated in a guard bed. If the deactivation is permanent, non-catalytic routes or more robust catalysts may need to be explored.

Splits and product specifications

Splits and product specifications are used to determine the number of outlet streams and the location of the product stream. A split refers to the action of separating the components of a mixture into two products, which could be either pure or a mixture (Fidkowski, 2006). Depending on the component distribution, a split can be sharp (each component appears only in one product), or non-sharp (each component appears in both products) (Fidkowski, 2006). Two criteria are used to define splits: the nature of the component and the boiling point order. The nature of the component refers to the role of each component in the reaction-separation system following the definition provided in our work about operating windows (Pazmiño-Mayorga et al., 2023): reactants, products, intermediate products, byproducts, or impurities (which could be reactive or inert). Then, boiling points at a specified pressure (e.g., atmospheric) allow the components to be arranged from the lightest to the heaviest. If the operating pressure is likely to differ significantly from atmospheric, the boiling point order may need to be revisited. At this point, azeotropes are not considered because they are analysed in the vapour-liquid equilibrium step.

If an intermediate boiling component is to be removed, two splits around the component are necessary to ensure the required specification. Figure 5.4 and the following guidelines help to identify the splits (number of streams).

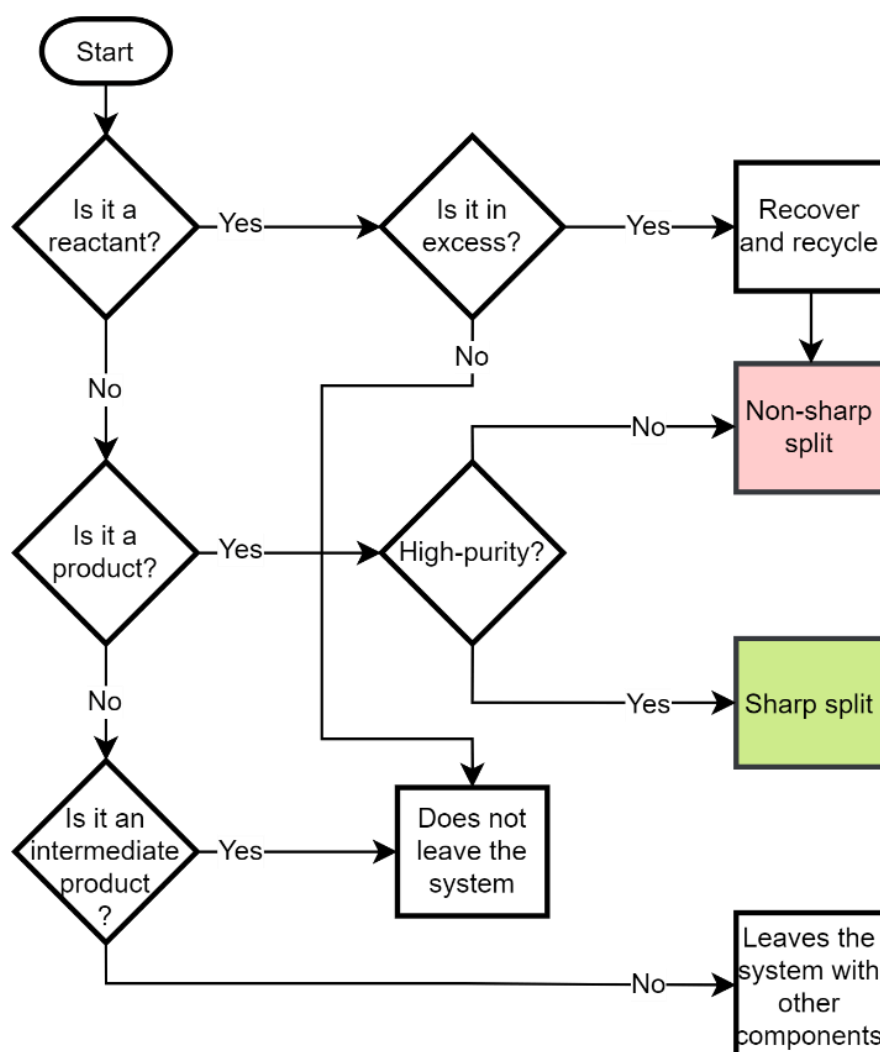


Figure 5.4. Flowchart to identify splits

- Reactants in excess need to be recovered and recycled. A non-sharp split suffices as long as there is no substantial recycling of components that can build up in the system. Incomplete conversion due to the equilibrium limitations could also be considered.
- To meet the product specifications, when high purity is required, one should aim for a sharp split; otherwise, a non-sharp split may suffice. Determining the type of split can guide the definition of operating parameters or design specifications when performing a detailed design in a later stage.
- Limiting reactants and intermediate products remain inside the ARDT device.
- Byproducts and impurities could be removed together.

Two product streams are easily managed in R-HiGee, R-HiDiC and CCD, whereas an R-DWC or MA-RD allow the withdrawal of three product streams. If the system has four or more streams, additional separation may be needed to achieve all the splits.

Finally, the location of the product cut can influence the selection of technologies because the withdrawal of a concentrated stream of the middle-boiling component in an R-DWC avoids remixing effects and results in higher purities compared to a conventional RD (Weinfeld et al., 2018).

5.2.4.3.2 Step 2. Basic properties and operating windows

Two data sets required for the second step include saturation temperatures at different pressures and materials and experimental methods constraints. These data are used to evaluate ARDT, as detailed in a previous study that introduces the concept of 'representative components' and the use of 'sliding windows' to add flexibility to the boundaries of the operating window (Pazmiño-Mayorga et al., 2023). Among the 'representative components', the lightest and heaviest are the light representative and the heavy representative components; these define boundaries to the operating window. Also, the reaction rate constant (discussed in detail in Step three) is included when building the operating window to identify temperature limits that might help prevent undesired side reactions.

The main findings of the operating windows are the operation boundaries for pressure and temperature and the definition of the temperature difference between the light and heavy representative components (ΔT_b) as a characteristic value for the chemical system (Figure 5.5). Results guiding the selection of technologies are based on the operating pressure and ΔT_b .

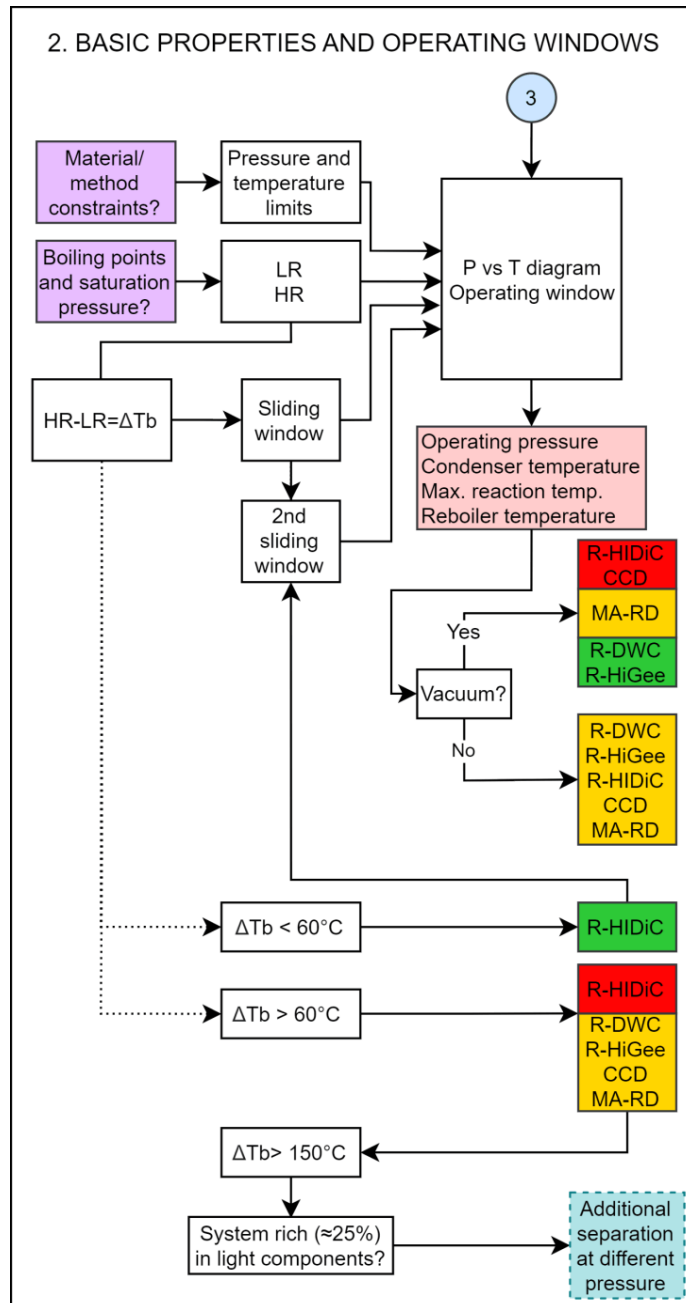


Figure 5.5. Step two: basic properties and operating windows flowchart

Operation below atmospheric pressure is not possible for R-HiDiC and CCD because of hardware limitations. For MA-RD, operation at or above atmospheric pressure is preferred because a stream at sub-atmospheric pressure may lead to engineering challenges for membrane operation. Regarding ΔT_b , heuristics from applications in non-reactive distillation technologies are used to provide reference values to navigate the decision-making flowchart. When ΔT_b is lower than 60°C, vapour recompression and internal heat integration could prove advantageous for close boiling component systems because economic compression costs could be achieved (Kiss and Olujić, 2014). When ΔT_b varies between 60 and 150°C, MA-RD, CCD, R-HiGee and R-DWC could potentially cover the range of temperatures required.

However, when ΔT_b is larger than 150°C and a relatively large amount of light components is present (~25%), an additional separation unit at different pressure may be needed to avoid incurring excessive costs due to a refrigerated condenser (Masel et al., 2013).

5.2.4.3.3 Step 3. Kinetics

The kinetic parameters – i.e., pre-exponential factor and activation energy – are used to determine the forward reaction rate constant of the main and relevant side reactions (Figure 5.6).

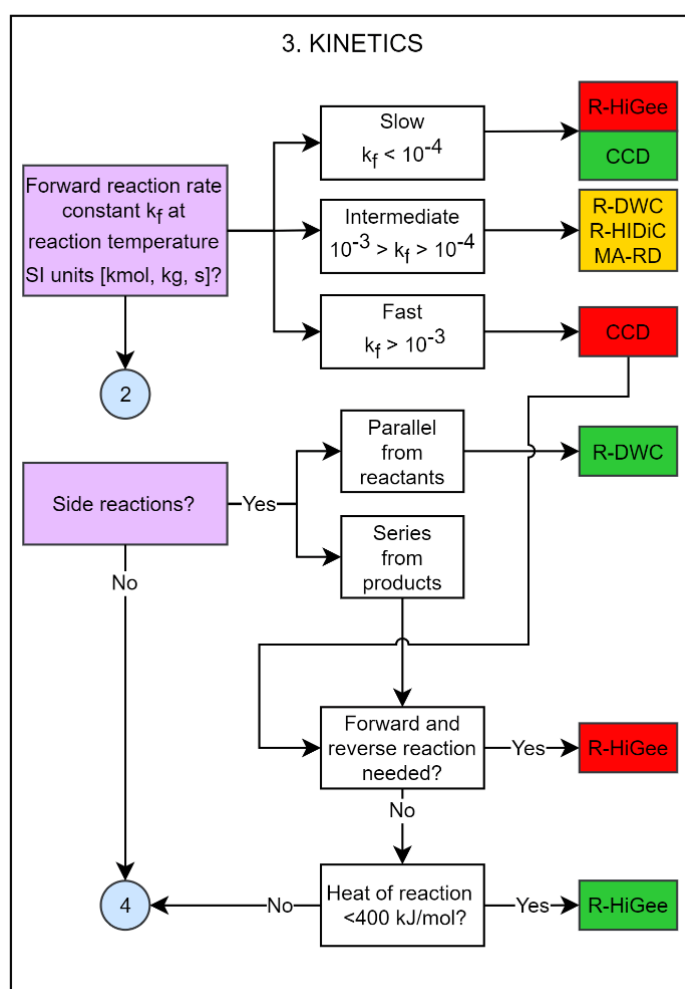


Figure 5.6: Step three: Kinetics flowchart

Forward reaction rate constant at the reaction temperature

Evaluating reaction rates is challenging due to factors influencing their values (e.g., initial concentrations, type of catalyst, solvents used, kinetic experiments, and regression models). Using absolute reaction rates does not allow performing a fair comparison between different chemical systems because reaction rates depend on concentrations (e.g., molar concentration, mole fraction, activities), order of the reaction, and the basis used, such as reaction volume or mass of catalyst. Therefore, the reaction rate constant expressed in SI units

(kmol, kg, s) is used as a reference to classify reactions as relatively slow, intermediate, or fast. The cutoff values were defined after a survey of previous works performed on RD (Luyben and Yu, 2008) and ARDTs to establish a range of reaction rates. Chemical systems tested in R-HiGee provided reference values for relatively fast reactions (Gudena et al., 2012; Schildhauer et al., 2009), while chemical systems tested in CCD provided reference values for relatively slow reactions (Lei et al., 2011). Initially, the reaction rate constant of the main reaction is evaluated at a given reaction temperature or at a reference temperature (e.g., a temperature that enhances the main reaction, maximum reaction temperature).

Fast reaction rates can take advantage of the short residence times in R-HiGee, enabling quick product removal (Quarderer et al., 2000; Schildhauer et al., 2009), while slow reactions are suited to CCD where the duration of the vapour flow period, when the reactions take place in the liquid phase, can be extended (Bîldea et al., 2017; Ortega et al., 2018).

Side reactions

Side reactions can occur in parallel or in series. Impurities, which normally accompany the main reactant in the feed stream, can promote parallel reactions when reactive. Series reactions depend on the chemical stability of the reaction products and can consume valuable products from the main reaction. Some parallel reactions can be avoided by adjusting the composition of the liquid phase. This modification is possible by locating feed and draw streams appropriately, taking advantage of the features of an R-DWC. For example, byproduct formation can be inhibited through recycling some byproduct or allowing buildup in the system, hence shifting the equilibrium (Smith, 2016). Some series reactions can be prevented by the rapid removal of reaction products, such as in an R-HiGee. However, the poor heat transfer in R-HiGee may not allow high heats of reaction to be accommodated (van der Schaaf and Schouten, 2011).

A special application of RD for fluid separations is when a 'reactive separating agent' is introduced to promote an equilibrium-limited reaction, where the products of the forward reaction are easy to separate; the reverse reaction can then be promoted to recover the component of interest (Pazmiño-Mayorga et al., 2023). Such a dual reactive separation system can be engineered to provide sufficient residence time, taking into account the volume occupied by the catalyst. R-HiGee is unlikely to be suited to the use of reactive separation agents due to its short residence times.

5.2.4.3.4 Step 4: Phase equilibrium

Especially in systems with non-ideal liquid phase behaviour, separations may be difficult (e.g., azeotropes may form). Data about azeotropes that form can provide insights into the thermodynamic constraints of a given system. RD technologies offer advantages in such non-ideal systems, compared to a conventional reaction-separation flowsheet, because azeotropes can be 'reacted away', facilitating required separations (Kiss, 2017).

This work compares data about azeotrope temperatures to boiling temperatures of the pure components, all arranged in order of increasing boiling point at a reference pressure (i.e., atmospheric). If the required split, identified in Step one, is away from the azeotrope, it is likely that the azeotrope could be reacted away if the reactive zone is located around the azeotrope temperature, hence facilitating separation. If the desired split is close to the azeotrope temperature, it is likely that the output stream contains the azeotrope, which would require additional techniques to break the azeotrope. In these cases, the azeotrope could be separated by using a different driving force. For example, MA-RD could be used if a suitable membrane is available. The flowchart in Figure 5.7 helps to identify azeotropes that can undermine the purity of the products; hence they need to be treated further.

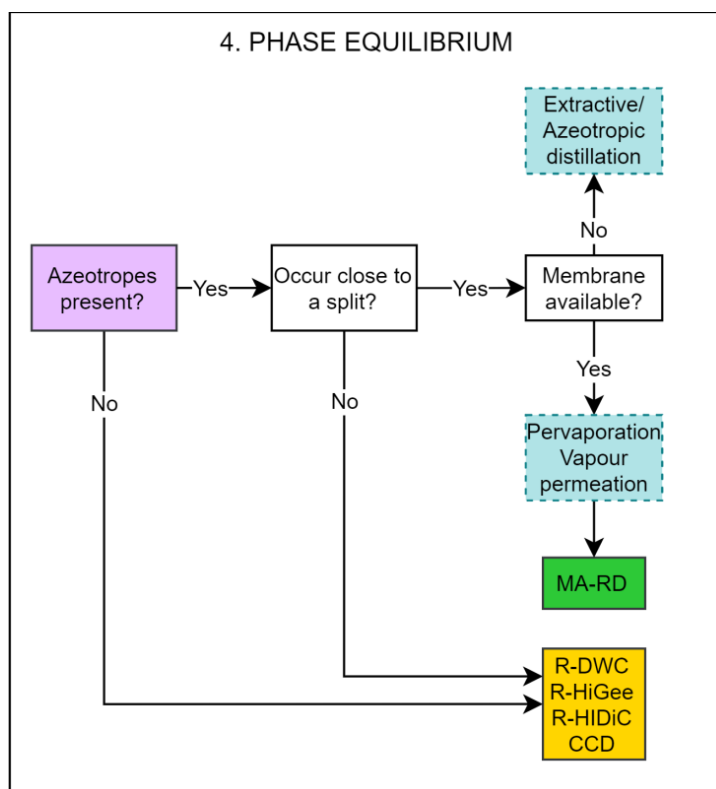


Figure 5.7. Step four: Phase equilibrium flowchart

In this work, systems with two or more liquid phases are not taken into account, given the sensitivity of liquid phase splitting to composition and operating conditions. Distillation regions and reactive azeotropes are not considered, despite their relevance (Doherty and Malone, 2001). This is because more detailed information regarding azeotrope compositions and their variation with operating conditions and experimental data or methods to identify reactive azeotropes are limited. A deeper examination of these characteristics is recommended after initial screening has revealed potential advantages and shortcomings.

5.2.4.4 Selection of advanced reactive distillation technologies

The results of the steps in the synthesis methodology are summarised in a decision-making matrix to facilitate analysis collating all aspects in a single view. This allows a quick evaluation, categorizing the methodology outcomes qualitatively as advantageous, technically feasible or not applicable. Decision points aiding the selection of technologies are listed horizontally (e.g., number of outlet streams, product cut location, vacuum operation, ΔT_b , reaction rate constant, side reactions and azeotropes), while ARDT options are listed vertically.

The applicability of each technology is indicated using a traffic light system according to the properties of the chemical system of interest and allows justifying important conditions to support the selection of technologies (Figure 5.2). Those technologies that have only green and amber indicators are identified as potentially advantageous, while those with mainly amber indicators are identified as technically feasible. Technologies with mainly red indicators are deemed not to be applicable. In the case that two technologies are deemed equally advantageous, they could be ranked by assigning a weight to each colour (e.g., green = 2, amber = 1), where the highest ranked are candidates for further investigation. Due to the qualitative nature of the approach, the results are not conclusive, but they provide a basis for further evaluation that is supported by a sound theoretical basis (thermodynamic properties and kinetic parameters) and heuristics as opposed to other more rigorous approaches, which are generally more complex and time-consuming (Martín and Adams, 2018). A conservative approach would have more stringent criteria, e.g., all indicators must be green, while a less conservative approach could shortlist both 'advantageous' and 'technically feasible' technologies. Additional technologies that could complement ARDT operation are suggested in dashed-lined boxes, which are indicated in an additional column in the decision-making matrix.

5.2.5 Case studies to demonstrate the application of the synthesis methodology

The synthesis methodology is applied to five case studies, aiming to identify suitable ARDT using basic thermodynamic properties and kinetic parameters. The results are compared to flowsheets studied quantitatively in the literature in order to check whether the outcomes of the methodology, using only basic information, are potentially realizable. Background information required to answer high-level questions is provided in the Supplementary Information for each case study. The outcomes of the methodology, summarised in the decision-making matrix, are illustrated in a process flow diagram (PFD) showing a potential configuration and the range of operating conditions (obtained from the operating windows).

5.2.5.1 Case 1: Purification of lactic acid

5.2.5.1.1 Description of the process and the design problem

Production of lactic acid has drawn the attention of academia and industry due to its applications in the food industry, pharmaceuticals, personal care, biodegradable polymers (e.g., polylactic acid) and as a building block molecule, where lactic acid is produced by fermentation of sugars (Alves de Oliveira et al., 2018). This case study focuses on the purification of lactic acid from a mixture containing reactive succinic acid and water as solvent.

The required separation is difficult; in this work, a reactive separating agent – methanol – facilitates the separation by promoting the esterification of lactic acid and succinic acid, where the products (methyl lactate and dimethyl succinate) can be separated by distillation. Once the heavy succinates are removed, the reverse reaction – hydrolysis – uses water to convert methyl lactate into lactic acid, now free from the impurity. Problem data are provided in the Supplementary Information in Table S5.13 and equations (24) to (28).

5.2.5.1.2 Methodology application and outcomes

The feed consists of lactic acid, substantial amounts of water and succinic acid, a reactive impurity (Table S5.14 in Supplementary Information).

- Step 1: water is inert; it acts as a solvent and can be partially removed. Remaining water must be removed to meet product specifications; while adjusting the composition of the liquid phase to promote hydrolysis to obtain lactic acid back after the impurity has been removed. Succinic acid is prone to side reactions and needs to be considered because it is a reactive impurity. Table 5.1 lists the components in order of increasing boiling point, their nature, and the desired splits: methanol is recycled; water is removed in pre-

concentration and downstream steps; byproducts and unreacted succinic acid are removed before hydrolysis, where methyl lactate is the dominant species; lactic acid is recovered after hydrolysis. The flowchart identifies R-DWC and MA-RD as potentially attractive candidates, but additional separation units would be needed to obtain the required product streams. R-DWC enables the removal of intermediate-boiling lactic acid as a side stream.

Table 5.1. List of components, nature and splits for the lactic acid system

Component	Nature	NBP (°C)	Output stream ^a
Methanol (LR)	Reactant	64.5	8
Water	Reactive impurity/ Intermediate product	100.0	2, 9
Methyl lactate	Intermediate product	144.8	–
Dimethyl succinate	Byproduct	196.4	7
Dilactic acid	Byproduct	215.9	7
Lactic acid (HR)	Reactant/ Product	216.6	6
Monomethyl succinate	Byproduct	222.6	7
Succinic acid	Reactive impurity	317.6	7
Trilactic acid	Byproduct	345.9	7

^a Streams numbers correspond to the flowsheet in Figure 5.8.

- Step 2: methanol and lactic acid are identified as the light and heavy representative components, respectively (Pazmiño-Mayorga et al., 2023). The suggested operating pressure ranges from 0.35 and 0.83 atm to avoid degradation of succinic acid. Technologies suitable for vacuum operation are R-DWC and R-HiGee, while MA-RD presents challenges. R-HiDiC and CCD are not applicable for vacuum operation. The ΔT_b is about 152°C at atmospheric pressure. Therefore, R-DWC, R-HiGee, CCD or MA-RD would need additional separation units.
- Step 3: methyl lactate production (main reaction) has an intermediate-to-fast reaction rate, while the reaction producing succinates (byproducts) is slower. Hence, the intermediate and fast ranges are selected. The side reaction between methanol and succinic acid occurs in parallel, which consumes the reactive separating agent. To suppress the esterification of succinic acid, side draws in an R-DWC can be advantageous to modify the composition of the liquid phase in a given stage, hence modifying the driving forces for the reaction. The oligomerisation of lactic acid occurs in series, where R-HiGee could potentially hinder this reaction. However, in the special case where the forward and reverse reactions are required, R-HiGee may not be able to provide enough residence time.

- Step 4: the system contains five homogeneous azeotropes (Table S5.15 in the Supplementary Information). Azeotropes between lactic acid and succinates are potentially problematic. However, succinates are produced in parallel with methyl lactate, and the heavier succinates can be removed before hydrolysis. Then, lactic acid is produced in the absence of succinates. Azeotropes that are away from the splits can be consumed within the reactive section of R-DWC, R-HiGee, CCD, and R-HiDiC. Figure S5.14 in the Supplementary Information illustrates the application of the flowchart; the outcomes are summarised in the matrix presented in Table 5.2.

Table 5.2. Decision-making matrix for the lactic acid system

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	⚡	✅	✅	⚡	⚡	✅	⚡	Advantageous	i, iii, iv
R-HiGee			✅	⚡	❌	❌	⚡	Not applicable	i, iii
R-HiDiC			❌	❌	⚡		⚡	Not applicable	i, iii
CCD			❌	⚡	❌		⚡	Not applicable	i, iv
MA-RD	⚡		⚡	⚡	⚡			Feasible	i, iii, iv

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

The flow diagram in Figure 5.8 – an R-DWC with auxiliary units – is proposed, based on the above findings. The method identifies the range of operating conditions – maximum temperature in the reactive section of 150°C, operating pressures between 0.35 and 0.83 atm, a condenser temperature between 40 and 60°C and a reboiler temperature between 192 and 212°C (Pazmiño-Mayorga et al., 2023).

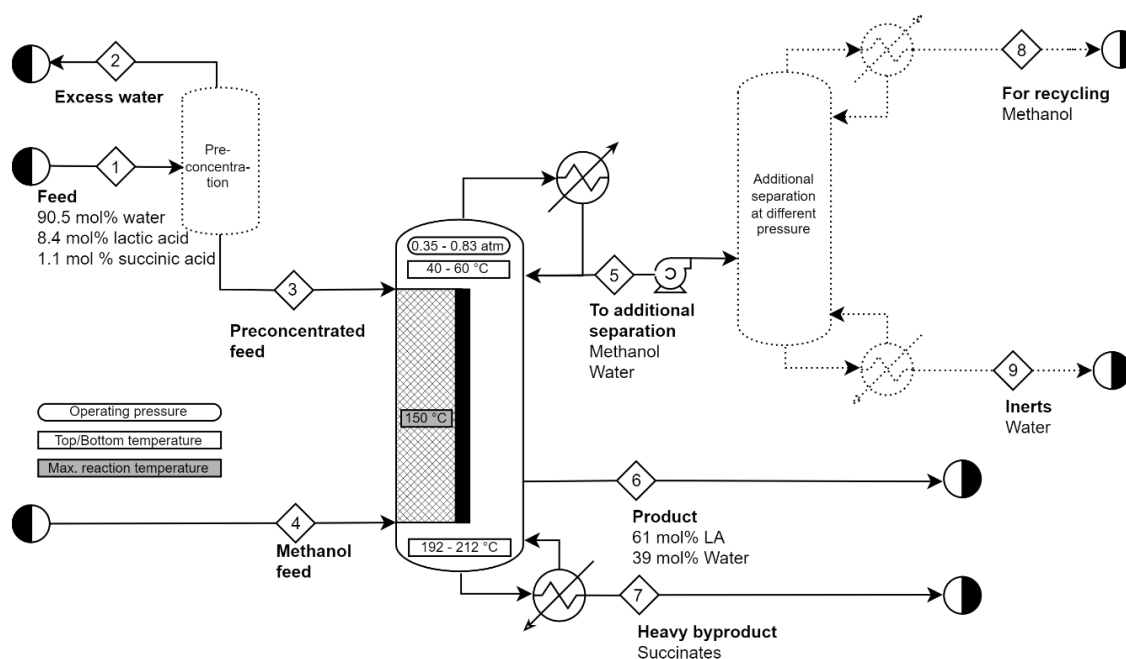


Figure 5.8. PFD for the lactic acid system including additional equipment (indicated with dotted lines)

R-DWC is deemed potentially advantageous: the side draw provides the main product, operation is under vacuum and undesired parallel reactions are hindered. The need for additional separation units is identified, to meet product specifications, and to remove impurities and water. These preliminary results clearly identify the ARDT with the best potential to satisfy the design problem among the technologies studied because the synthesis methodology was able to eliminate those potentially unfeasible from the evaluation.

5.2.5.1.3 Comparison of the results of the methodology with the literature

The advantages of R-DWC agree with those observed in earlier studies. For example, simulation studies found that R-DWC and thermally coupled arrangements are advantageous in terms of energy use when compared to conventional RD (Cho et al., 2008; Kim et al., 2017). In addition, our previous conceptual design study helped identify the benefits of a dual R-DWC by using detailed kinetics for the main and side reactions in a rigorous simulation. The configuration improved energy use, material intensity, and water consumption (Pazmiño-Mayorga et al., 2021). MA-RD could be used but with no specific advantage, except for the case where an azeotrope needs to be dealt with and if a suitable membrane exists.

R-HiGee, CCD and R-HiDiC are discarded. Gudena et al. (2013b) evaluated methyl lactate hydrolysis in an R-HiGee stripper-membrane process, so this study is used to verify the outcomes of the methodology. The hydrolysis of methyl lactate, which is needed to recover lactic acid after impurities removal, is slower than the esterification of lactic acid. Gudena et al. (2013b) concluded that a relatively long residence time is necessary to achieve higher conversion for the substrate. In addition, a decrease in feed conversion and a marginal increase in operating cost were observed compared to a conventional reactive stripper coupled to a membrane. When evaluating kinetics in the proposed synthesis methodology, both the forward and reverse reactions were considered, which allowed identifying R-HiGee as unsuitable for a special case when both reactions are needed. Finally, the main limitation of applying R-HiDiC and CCD depends on the inability to operate in a vacuum.

5.2.5.2 Production of dimethyl ether (DME)

5.2.5.2.1 Description of the process and the design problem

DME is typically produced in a catalytic fixed-bed reactor at high-pressure. Table S5.16 in the Supplementary Information provides an overview of the DME system. The feed consists of pure methanol, which is dehydrated to produce DME and water (equation (29) in the

Supplementary Information). Numerical values used as inputs for the application of the methodology are provided in Table S5.17 in the Supplementary Information.

5.2.5.2.2 Methodology application and outcomes

- Step 1: the feed is pure methanol, so no interactions are expected apart from the main reaction to obtain DME (equation (29) in the Supplementary Information). Two outlet streams are expected since full conversion of methanol is assumed, and DME is the lightest compound that could be recovered from the top of the column. The list of components in order of increasing boiling point and their nature are provided in Table 5.3.

Table 5.3. List of components, nature and splits for the DME system

Components	Nature	NBP (°C)	Output stream ^a
Dimethyl ether (LR)	Product	-24.8	2
Methanol	Reactant	64.7	–
Water (HR)	Byproduct	100.0	3

^a Streams numbers correspond to the flowsheet in Figure 5.9.

- Step 2: DME and water are the light and heavy representative components, and their vapour pressure curves provide boundaries for the operating window (Pazmiño-Mayorga et al., 2023). Relatively high operating pressures (8.8 to 14.3 atm) are required because of the high volatility of DME. Therefore, all ARDT are suited for operation above atmospheric. The ΔT_b is 125°C at atmospheric pressure, so R-DWC, R-HiGee, CCD and MA-RD could operate without further separation.
- Step 3: the reaction rate constant at 90°C indicates that the reaction is relatively slow, suggesting CCD due to larger residence times, thus ruling out R-HiGee. The system does not present side reactions.
- Step 4: the system does not present azeotropes; hence there is no restriction for R-DWC, R-HiGee, CCD or R-HiDiC. The ternary diagram showed an envelope where two liquid phases co-exist (Park et al., 2007), when the mixture is lean in methanol, which is unlikely. However, the effect of this miscibility gap could be further explored in a more detailed study.

The decision-making flowchart is shown in Figure S5.15 in the Supplementary Information. The decision-making matrix in Table 5.4 indicates that CCD could be advantageous for the production of DME due to the relatively slow reaction rate, while R-DWC and MA-RD are technically feasible. R-HiGee and R-HiDiC are discarded.

Figure 5.9 presents a potential configuration for the production of DME, including the operating conditions found from the operating window. The maximum temperature in the reactive section is 150°C, and the top and bottom temperatures are 40–60°C and 165–185°C, respectively. The range of operating pressures is 8.8 to 14.4 atm.

Table 5.4. Decision-making matrix for the DME system

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC			⬆	⬆		-	⬆	Feasible	-
R-HiGee	⬆	⬆	⬆	⬆	✗	-	⬆	Not applicable	-
R-HiDiC	⬆	⬆	⬆	✗		-	⬆	Not applicable	-
CCD	⬆	⬆	⬆	⬆	✓	-	⬆	Advantageous	-
MA-RD			⬆	⬆		-		Feasible	-

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

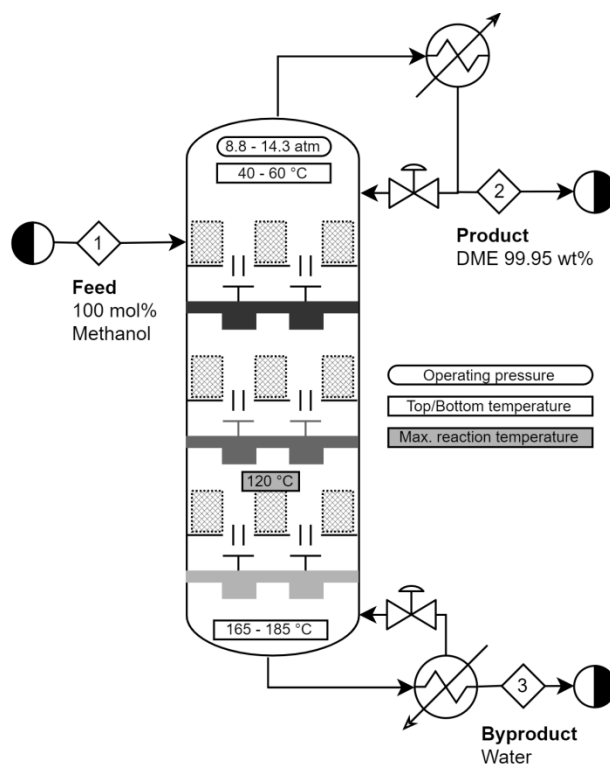


Figure 5.9. PFD for the DME system

This case study is relatively straightforward to analyse due to the small number of components involved, no side reactions and no azeotropes. Although the decision-making matrix shows feasibility for all ARDT in most decision points, the rate of reactions is decisive in identifying CCD as advantageous and discarding R-HiGee. R-HiDiC is also discarded as the temperature ranges may incur high compression costs.

Taken together, these results suggest that CCD is advantageous based on the reaction rate criterion, but R-DWC and MA-RD are technically feasible based on other characteristics. This

case study raises the possibility of various process alternatives being suitable if the answers to decision points change. For example, accelerated reaction with a different catalyst, partial conversion where unreacted methanol needs to be recovered, and the miscibility gap already identified but not considered in the analysis.

5.2.5.2.3 Comparison of the results of the methodology with the literature

In accordance with these results, previous studies have shown that different technologies could successfully produce DME depending on aspects not included in the context of the proposed synthesis methodology (e.g., retrofit vs new design), allowing alternative processing options depending on the context. For example, Bîldea et al.(2017) found RD to be particularly useful for revamping existing plants.

Conceptual design studies for the production of dialkyl ethers, including DME, indicated that – compared to conventional RD – CCD could achieve higher product purities while reducing the number of stages and vapour flowrate (Kiss et al., 2015; Pătruț et al., 2014). Rasmussen et al. (2022) analysed the production of DME using quantitative metrics to evaluate the performance of CCD, including the mean Damköhler number, which accounts for characteristics of the technology.

Conceptual design studies corroborate the feasibility of R-DWC (Gor et al., 2020; Kiss and Suszwalak, 2012). Kiss and Suszwalak (2012) proposed an R-DWC operating at 10 bar that showed energy savings compared with conventional RD. Gor et al. (2020) found that RD presents 10.68 % less total annualised costs (TAC) than an R-DWC operating at 9 to 10 bar with two reactive sections, one at each side of the wall. This apparent discrepancy may be explained by the scope of the analysis, where Kiss and Suszwalak (2012) use energy use (i.e., operating costs) as an indicator, whereas Gor et al. (2020) included capital costs. In addition, both RD and R-DWC performed better than conventional configurations (Gor et al., 2020). A compromise between the integration of functionalities and the ease of implementation is still being evaluated for RD, which depends heavily on the type of catalyst used, hence on the reaction kinetics (Bîldea et al., 2017; Gor et al., 2020).

Regarding MA-RD, a pervaporation-assisted RD configuration presented promising results in terms of TAC compared to a conventional RD column (Liu et al., 2022). In summary, the proposed synthesis methodology suggests technologies that are worth exploring further, denoting aspects that could be adjusted to overcome a limitation, such as catalyst robustness.

For example, Su et al. (2016) proposed a dual R-DWC that uses two reaction zones with catalysts that withstand different temperatures to enlarge the catalyst life.

5.2.5.3 Production of tert-amyl methyl ether (TAME)

5.2.5.3.1 Description of the conventional process

TAME is a fuel additive produced from the addition of isoamylenes to methanol. The FCC unit in an oil refinery provides the feed stream that contains inert alkanes, olefins, cyclic components and sulphur. In the Supplementary Information, Table S5.18 presents an overview of the TAME system, while Table S5.19 provides numerical values applied in the methodology and the reactions involved are presented in equations (30) to (35).

5.2.5.3.2 Methodology application

The design problem involves the transformation of isoamylenes into TAME while dealing with large amounts of inert materials, potential side reactions and unwanted byproducts. The main reactions are TAME formation from isoamylenes 2M1B and 2M2B, and one isomerisation reaction between 2M1B and 2M2B, which are equilibrium-limited (Luyben and Yu, 2008). Possible side reactions include the formation of dimers and trimers of 2M1B and 2M2B (Cruz et al., 2007) and methanol condensation to DME (Subawalla and Fair, 1999). All reactions are given in equations (30) to (35) in the Supplementary Information. Most simulation studies omit side reactions in their models, but investigating the effect of side reactions is necessary because they can affect operation. Therefore, two scenarios are evaluated to apply the synthesis methodology: Scenario 1 considers the main reactions only (equations (30–32)) and Scenario 2 accounts for side reactions also (equations (30–35)).

Scenario 1: TAME production disregarding side reactions

- Step 1: Table 5.5 lists the components in order of increasing boiling point, their nature, and notes the light and heavy representative components. Pre-removal of inert materials is difficult due to their close boiling points, so the expected outlet streams include impurities removal.

Table 5.5. List of components, nature and splits for the TAME system (Scenario 1)

Components	Nature	NBP (°C)	Output stream ^a
Isopentane (LR)	Inert impurity	27.8	3
1-pentene	Inert impurity	30.1	3
2M1B	Reactant	31.2	–
2M2B	Reactant	38.6	–
Cyclopentane	Inert impurity	49.3	3
Methanol	Reactant	64.7	4 ^b
TAME (HR)	Product	86.4	5

^a Streams numbers correspond to the flowsheet in Figure 5.10.^b when methanol is fed in excess

- Step 2: the ΔT_b is 60°C, which indicates that an R-HiDiC could provide advantages. Our previous publication about operating windows (Pazmiño-Mayorga et al., 2023) found the operating pressure to be between 0.11 and 4.4 atm for the stripping section and between 1 and 13.2 atm for the rectifying section. Although the range of pressures found for the stripping section covers values below and above atmospheric, only pressures above atmospheric are considered here as they account for the largest range of operating conditions.
- Step 3: the reaction rate constant at 90°C has a magnitude of 10^{-3} , which allows the application of R-HiDiC, R-DWC and MA-RD.
- Step 4: Scenario 1 features seven azeotropes detailed in Table S5.20 in the Supplementary Information. Most azeotropes occur with methanol, and of particular interest is the low-boiling azeotrope formed between methanol and TAME. This azeotrope is problematic because it occurs next to a desired split so that a membrane module could be used in an MA-RD column. Several studies applying pervaporation to deal with the methanol-TAME azeotrope have been investigated (Hung et al., 1998; Marx et al., 2002, 2005).

Scenario 2: TAME production considering side reactions

Scenario 2 considers series reactions producing dimers, trimers and methanol condensation producing (DME) and water. A characteristic dimer is 2,3,4,4-tetramethyl-1-hexene, which promotes the production of 2,4,6,6,7,7-hexamethylnon-3-ene (characteristic trimer). The components in Scenario 2 are shown in Table 5.6.

Table 5.6. List of components, nature and splits for the TAME system (Scenario 2)

Components	Nature	NBP (°C)	Output stream ^a
DME	Byproduct	-24.8	7 ^b
Isopentane (LR)	Inert impurity	27.8	6
1-pentene	Inert impurity	30.1	6
2M1B	Reactant	31.2	—
2M2B	Reactant	38.6	—
Cyclopentane	Inert impurity	49.3	6
Methanol	Reactant	64.7	8 ^b
TAME (HR)	Product	86.4	9
Water	Byproduct	100.0	4 ^b
Dimer	Byproduct	155.2	4
Trimer	Byproduct	256.8	4

^a Streams numbers correspond to the flowsheet in Figure 5.11.^b when methanol is fed in excess

- Step 1: extra outlet streams are needed due to the additional byproducts. R-DWC or MA-RD allows at least three outlet streams. Because of heavy byproducts, the product stream is an intermediate cut, the removal of which is facilitated in an R-DWC.
- Step 2: the light and heavy representative components identified are isopentane and TAME. Due to the large activation energy, the reactions producing DME and oligomers are likely to be slower than the main reactions. ΔT_b is about 60°C, which could find advantages in the application of R-HiDiC.
- Step 3: the reaction rate constant is in the intermediate range, so R-HiDiC, R-DWC and MA-RD are recommended. Oligomerisation reactions occur in series and are slower than the etherification reaction, so reducing the contact time will reduce the likelihood of producing dimers and trimers in an R-HiGee. Conversely, dehydration of methanol occurs in parallel and using R-DWC could be advantageous.
- Step 4: additional byproducts result in additional azeotropes. Scenario 2 features 17 azeotropes mainly formed with either methanol or water (Table S5.21 in Supplementary Information). Four homogeneous azeotropes and 13 heterogeneous azeotropes have two or three components. A membrane – in an MA-RD – could deal with the azeotropes between TAME and methanol and between TAME and water that are located near the split to recover the main product.

5.2.5.3.3 Methodology outcomes

The decision-making flowchart for Scenario 1 is illustrated in Figure S5.16 in the Supplementary Information, and the results are summarised in the decision-making matrix in Table 5.7. R-HIDiC and MA-RD show benefits for the system. Particularly, R-HIDiC is able to exploit the small ΔT_b .

Table 5.7. Decision-making matrix for the TAME system (Scenario 1)

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	⚠		⚠		⚠	-		Feasible	vi
R-HiGee		⚠	⚠			-		Feasible	vi
R-HIDiC		⚠	⚠	✓	⚠	-		Advantageous	vi
CCD		⚠	⚠			-		Feasible	vi
MA-RD	⚠		⚠		⚠	-	✓	Advantageous	

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

First, Figure 5.10 (a) presents a potential flowsheet of an R-HIDiC, including a membrane module to deal with the methanol-TAME azeotrope in case of excess methanol. The low-pressure section – stripping section – could operate between 0.11 and 4.4 atm, and the high-pressure section operates between 1 and 13.2 atm. The maximum reaction temperature is 150°C. The range of temperatures in both sections overlaps, which could initially suggest that heat transfer is not possible. However, temperature profiles depend on the selected operating pressure and the pressure ratio. Second, Figure 5.10 (b) proposed a potential flowsheet including an MA-RD with operating conditions evaluated in a single operating window, where the operating pressure ranges between 1.5 and 7.3 atm. In both flowsheets, the dotted lines for the membrane module and the methanol stream indicate that they occur when excess methanol is fed.

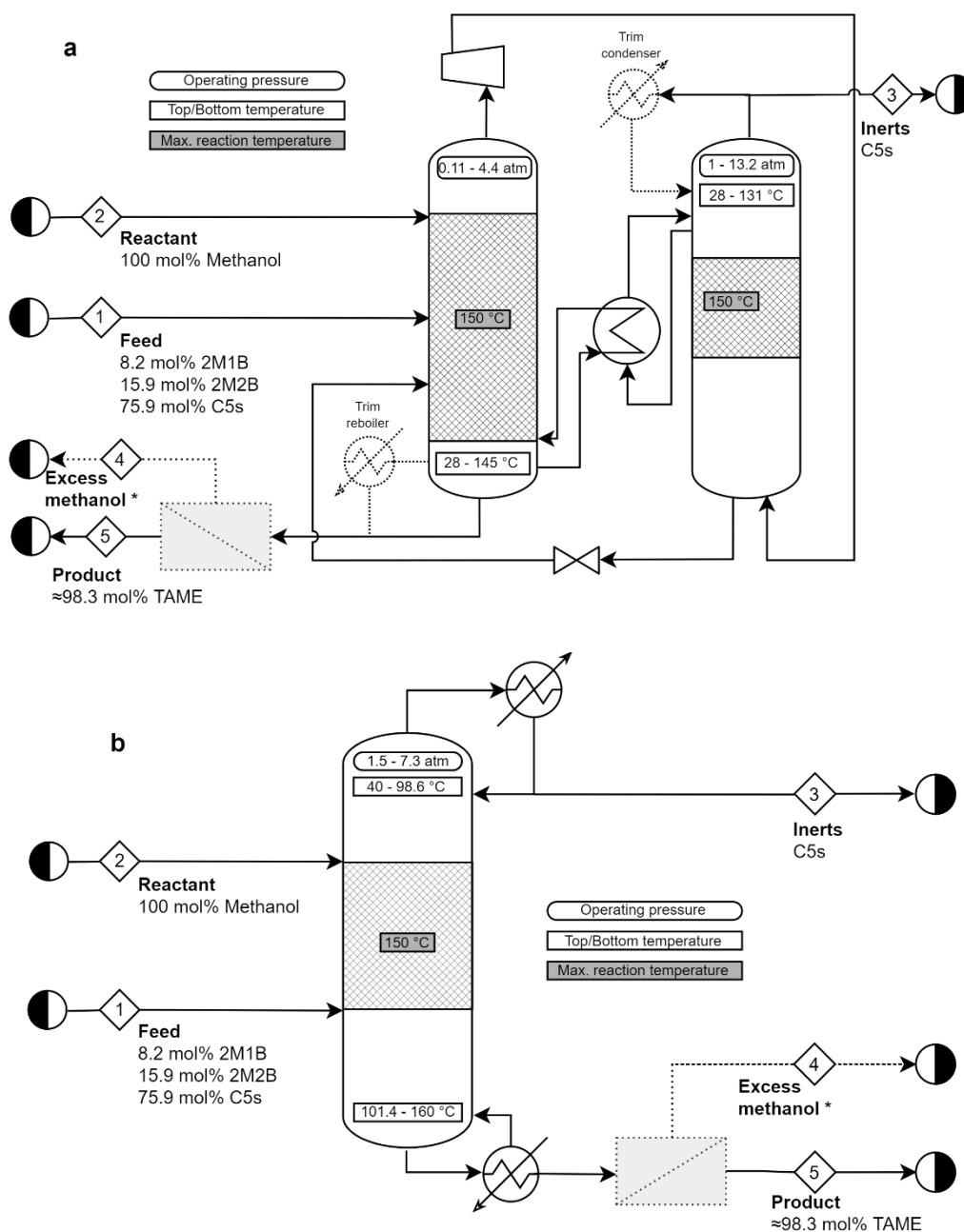


Figure 5.10. PFD for the TAME system (Scenario 1) for an R-HIDiC configuration including a membrane module (a) and a MA-RD (b) (*when excess methanol is fed to the system)

When considering side reactions in Scenario 2, additional species emerge. The application in the decision-making flowchart is illustrated in Figure S5.17 in the Supplementary Information. The outcomes of the methodology are summarised in the decision-making matrix in Table 5.8.

Table 5.8. Decision-making matrix for the TAME system (Scenario 2)

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	!	✓	!		!	✓		Advantageous (Rank 1)	iii, vi
R-HiGee			!			✓		Advantageous (Rank 4)	iii, vi
R-HiDiC			!	✓	!			Advantageous (Rank 3)	iii, vi
CCD			!					Feasible	iii, vi
MA-RD	!		!		!		✓	Advantageous (Rank 2)	iii

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

Side reactions (both in series and in parallel) and heavy byproducts make the R-DWC appear as the most advantageous technology, followed by MA-RD, R-HiDiC and R-HiGee. Product location and parallel reactions are the main drivers for the use of R-DWC. Due to the additional streams that need to be removed and the problematic azeotropes around the product stream, an additional separation unit and a membrane module are suggested as auxiliary units, illustrated in Figure 5.11. Potential operating conditions are pressure between 2.7 and 10.9 atm, with a condenser temperature between 60 to 121°C and a reboiler temperature between 119 and 180°C. The reaction window is reduced since temperatures between 110 and 150°C favour main reactions over side reactions (Pazmiño-Mayorga et al., 2023). By analysing the lightest components in the system, DME and isopentane could be easily separated in a flash vessel due to the large temperature difference between them and the absence of azeotropes. At the heaviest end of the mixture, separation is more challenging due to a heterogeneous azeotrope between TAME and water.

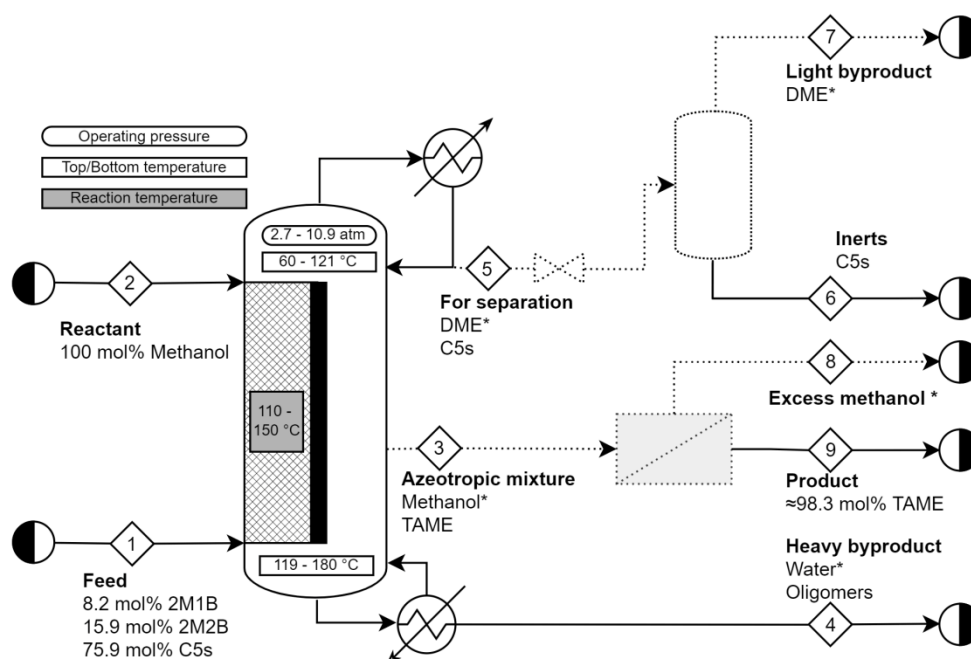


Figure 5.11. PFD for the TAME system (Scenario 2) for an R-DWC including a membrane module and a flash separation (*when excess methanol is fed to the system)

DME production – hence water – occurs at high methanol-to-feed ratios and high temperatures (Boz and Dogu, 2005; Kołodziej et al., 2004). Therefore, operating close to the stoichiometric ratio could help to avoid producing DME and water (marked with an asterisk in Figure 5.11). If methanol remains in the system, it will need to be recovered and recycled with additional units (denoted with dotted lines).

This case study was designed to identify the effect of side reactions in technology selection. First, byproducts require to be removed; hence the number of streams and the location of the product cut change. Second, the decision point accounting for side reactions suggests technologies that could be advantageous to overcome the challenges in Scenario 2.

5.2.5.3.4 Comparison of the results of the methodology with the literature

R-HIDiC and MA-RD are advantageous in both scenarios. Although there is no apparent winner for Scenario 2, R-DWC provides additional features that allow for overcoming issues of a more complex system. These findings, along with the reduction of the reaction window identified (Pazmiño-Mayorga et al., 2023), demonstrate that the effect of side reactions could be detected in an early stage and influence the selection of technologies.

For Scenario 1, R-HIDiC shows advantages due to the small ΔT_b . The potential of R-HIDiC is corroborated by published simulation studies (Gao et al., 2014; Pulido et al., 2011; Vanaki and Eslamloueyan, 2012). Babaie and Nasr Esfahany (2020) added a pervaporation module to R-HIDiC to overcome the azeotrope between (unreacted) methanol and isopentane. This result agrees with the suggestion of an additional membrane module to complement the operation of ARDT.

When accounting for side reactions in Scenario 2, R-DWC is suggested as the most advantageous, followed by MA-RD, R-HIDiC and R-HiGee. To date, no studies have included side reactions in simulations for conventional RD or ARDT. Therefore, further rigorous modelling studies for the production of TAME, including side reactions, are recommended to assess the impacts of side reactions on process performance.

5.2.5.4 Production of methyl acetate

5.2.5.4.1 Description of the process and the design problem

Methyl acetate industrial process is well known and has been thoroughly studied, hence the availability of data and various benchmark configurations (Bayer et al., 2002). One method for

methyl acetate production is the esterification of methanol and acetic acid. A general overview of the methyl acetate system is provided in Table S5.22, numerical values are included in Table S5.23, and reactions are given in equations (36–37) in the Supplementary Information.

5.2.5.4.2 Methodology application and outcomes

The feeds to the esterification process consist of pure acetic acid and a slight excess of methanol (Al-Arfaj and Luyben, 2002; An et al., 2015; Krishna et al., 2012; Pöpkén et al., 2001; Zuo et al., 2014).

- Step 1: components participating in the system, including byproducts from the dehydration of methanol, are listed in Table 5.9. Four outlet streams are expected, thus requiring an additional separation unit to complement the operation of R-DWC and MA-RD.

Table 5.9. List of components, nature and splits for the methyl acetate system

Components	Nature	NBP (°C)	Output stream ^a
Dimethyl ether	Byproduct	-24.8	1
Methyl acetate (LR)	Product	56.9	2
Methanol	Reactant	64.7	3
Water	Byproduct	100.0	4
Acetic acid (HR)	Reactant	117.9	–

^a Streams numbers correspond to the flowsheet in Figure 5.12

- Step 2: the ΔT_b is about 61°C at atmospheric pressure. ΔT_b is slightly larger than 60°C; hence, three scenarios were evaluated due to the closeness to the threshold value: a) two sliding windows for systems with a $\Delta T_b < 60^\circ\text{C}$, and one sliding window for systems with a $\Delta T_b > 60^\circ\text{C}$ where b1) operates at vacuum and b2) operates above atmospheric.
- Step 3: reactions involved are the esterification of acetic acid with methanol and the potential dehydration of methanol into DME, which are presented in equations (36) and (37) in the Supplementary Information. The reaction rate constant for the esterification of acetic acid calculated at 90°C and 120°C (maximum reaction temperature) has an order of magnitude of 10^{-3} , so the technologies suggested are R-DWC, R-HIDiC and MA-RD. Dehydration of methanol occurs in parallel with the esterification of lactic acid. Thus, R-DWC is recommended to deal with the side reaction.
- Step 4: the mixture is non-ideal and exhibits two low-boiling azeotropes: methyl acetate-methanol and methyl acetate-water (Ganesh et al., 2014). The normal boiling point and

type of azeotropes are detailed in Table S5.24 in the Supplementary Information. As a result, the ester product is usually removed as the methanol-methyl acetate azeotrope, whose treatment has been studied in various membrane applications (Abdallah et al., 2013; Ahmad et al., 2013; Genduso et al., 2015; Gorri et al., 2006; Y. Li et al., 2019; Lux et al., 2017; Penkova et al., 2013; Sain et al., 1998; Tong-Hu et al., 2011; Zong et al., 2021). Hence MA-RD could potentially be used.

Table 5.10 presents three decision-making matrices, denoting the alternatives found when evaluating basic properties and operating windows in Step two.

Table 5.10. Decision-making matrices for the methyl acetate system

a) $\Delta T_b < 60^\circ\text{C}$

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	⚠	✓	⚠		⚠	✓		Advantageous (Rank 1)	iii, vi
R-HiGee			⚠					Feasible	iii, vi
R-HiDiC			⚠	✓	⚠			Advantageous (Rank 3)	iii, vi
CCD			⚠					Feasible	iii, vi
MA-RD	⚠		⚠		⚠		✓	Advantageous (Rank 2)	iii

b1) $\Delta T_b > 60^\circ\text{C}$ with operation at vacuum

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	⚠	✓	✓	⚠	⚠	✓		Advantageous (Rank 1)	iii, vi
R-HiGee			✓	⚠				Advantageous (Rank 3)	iii, vi
R-HiDiC			✗	✗	⚠			Not applicable	iii, vi
CCD			✗	⚠				Not applicable	iii, vi
MA-RD	⚠		⚠	⚠	⚠		✓	Advantageous (Rank 2)	iii

b1) $\Delta T_b > 60^\circ\text{C}$ with operation above atmospheric

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	⚠	✓	⚠	⚠	⚠	✓		Advantageous (Rank 1)	iii, vi
R-HiGee			⚠	⚠				Feasible	iii, vi
R-HiDiC			⚠	✗	⚠			Not applicable	iii, vi
CCD			⚠	⚠				Feasible	iii, vi
MA-RD	⚠		⚠	⚠	⚠		✓	Advantageous (Rank 2)	iii

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

The three scenarios agree on identifying R-DWC and MA-RD as advantageous. In addition, case a) suggest using R-HiDiC to take advantage of the close boiling components. Case b1) operating at vacuum also suggests R-HiGee. Following well-known heuristics, avoiding vacuum conditions is desired; hence R-HiGee is unlikely to be necessary. Therefore, R-DWC, MA-RD and R-HiDiC represent advantageous processing options that could be further evaluated. Due to the number of outlet streams required and the azeotrope occurring close to the desired split, additional separation and the use of a membrane module can complement the operation.

Figure 5.12 presents the potential flowsheet configurations, including auxiliary equipment and operating conditions. The first ranked is an R-DWC including a membrane module (a), then an MA-RD including a flash separation unit (b) and finally an R-HIDiC including a flash separation unit and a membrane module when exploiting the closeness in boiling points (c).

This case study was proposed to demonstrate the flexibility of the synthesis methodology as the decision-making flowchart provides guidelines that could be adapted as the evaluation progresses. This is important because, from a practical point of view, the proposed approach allows potential processing options to be identified systematically. The methodology provides arguments as to why one technology might be advantageous while others are discarded according to the context and targets of the design problem. Although the results from evaluating operating windows that account for ARDT (Pazmiño-Mayorga et al., 2023) are preliminary for this case study, the observations provide valuable insights for selecting technologies, and the results are verified with published studies.

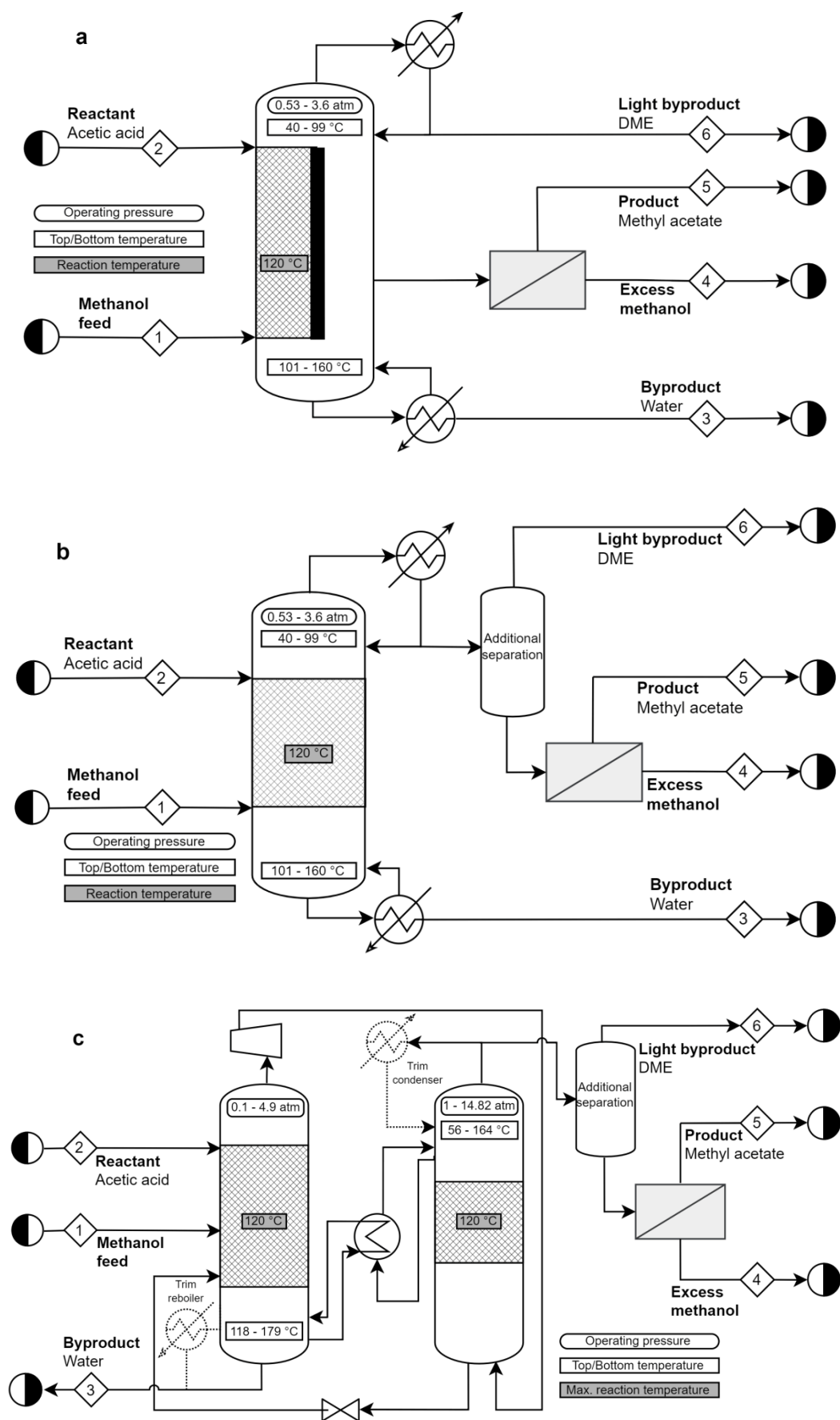


Figure 5.12. PFDs for the methyl acetate system: R-DWC (a), MA-RD (b) and R-HIDiC (c)

5.2.5.4.3 Comparison of the results of the methodology with the literature

The esterification of organic acids, particularly acetic acid, has been thoroughly studied in both traditional and hybrid processes (Bayer et al., 2002). Experimental and modelling studies have been performed, including control structures applied for RD applications (Al-Arfaj and Luyben, 2002; Babi et al., 2014; Ganesh et al., 2014; Luyben and Yu, 2008; Pöpkén et al., 2001). Aiming to improve the performance of RD, an R-DWC at atmospheric pressure presented benefits in terms of TAC compared to a sequence of RD and conventional distillation, and showed better dynamic performance than a single RD using a stoichiometric feed ratio (An et al., 2015). Integration of a membrane module to RD to overcome the methanol-methyl acetate azeotrope has not been described in the literature, although independent membrane studies have been performed (Abdallah et al., 2013; Genduso et al., 2015; Gorri et al., 2006; Y. Li et al., 2019; Lux et al., 2017; Tong-Hu et al., 2011). Babi et al. (2014) presented a synthesis-intensification framework that emphasises the importance of membranes to improve sustainability. However, ARDT were not included in the framework. Therefore, an interesting next step will be the study of an MA-RD for the production of methyl acetate, which could be compared with various configurations (conventional and intensified) to assess its benefits.

Finally, R-HIDiC was deemed advantageous when considering the closeness of boiling points. However, published studies have applied R-HIDiC to the hydrolysis of methyl acetate, which is the reverse reaction (Chen et al., 2020; Lee et al., 2010; Li et al., 2015; Zhai et al., 2015). The decision-making process for the hydrolysis of methyl acetate is detailed in the Supplementary Information in section 5.3.1.4.1, including the decision-making matrix and flowchart, highlighting decision points (e.g., change in product cut location, no side reactions, azeotrope located far from the split) that drive the selection of technologies in a different direction. From the comparison, the occurrence of DME with the esterification of acetic acid could affect the temperature profile along the column. Therefore, a light component could present challenges for the operation of the compressor. Further studies are recommended to assess the applicability of R-HIDiC for the esterification of acetic acid to assess the impact of the dehydration of methanol.

5.2.5.5 Production of cyclohexane

5.2.5.5.1 Description of the process and the design problem

Cyclohexane is an important raw material in the petrochemical industry, mainly obtained through benzene hydrogenation (Li et al., 2018). Separating benzene from cyclohexane is

challenging because of their close boiling points and azeotrope. Various techniques have been investigated for the separation of the benzene-cyclohexane mixture (Garcia Villaluenga and Tabe-Mohammadi, 2000; Xi et al., 2019; Zahlan et al., 2020; Zhang et al., 2020). Therefore, this case study explores the application of ARDT for a typical hydrogenation reaction. An overview of the cyclohexane system is summarised in Table S5.27 in the Supplementary Information.

5.2.5.5.2 Methodology application and outcomes

- Step 1: the benzene feed contains a considerable amount of C5–C9 paraffins and other aromatics, as detailed in Table S5.28 in the Supplementary Information. The feed is also likely to contain sulphur compounds, so a guard reactor can be used. Inert paraffins need to be removed, which is considered when defining the splits, while cumene tends to react with hydrogen – side reaction. Table 5.11 lists the components in order of increasing boiling point and denotes their nature. The most difficult split is to separate benzene and cyclohexane due to their close boiling points. Benzene can be fully or partially converted. If full conversion is achieved, no benzene will exit the system. However, if benzene is not fully converted, it is expected to exit the system along with cyclohexane. Due to the number of streams that need to be removed, an additional separation unit could complement the operation of ARDT. The product stream, cyclohexane, is mid-boiling, so the use of an R-DWC helps its removal as a side draw.

Table 5.11. List of components, nature and splits for the cyclohexane system

Components	Nature	NBP (°C)	Output stream ^a
Hydrogen	Reactant	-252.8	1
n-pentane (LR)	Inert impurity	36.1	2
Methyl cyclopentane	Byproduct	71.8	2
Benzene	Reactant	80.1	3 ^b
Cyclohexane	Product	80.7	5
2,3-dimethyl pentane	Inert impurity	89.8	4
n-heptane	Inert impurity	98.4	4
Methyl cyclohexane	Byproduct	100.9	4
Toluene	Reactive impurity	110.6	4
m-xylene	Inert impurity	139.1	4
Cumene (HR)	Inert impurity	152.4	4

^a Streams numbers correspond to the flowsheet in Figure 5.13.

^b when benzene is not fully converted

- Step 2: hydrogen is not considered as a representative component because it is a gas that will not condense, and its boiling temperature is far from that of other compounds. As a result, the light and heavy representative compounds are n-pentane and cumene,

respectively. The ΔT_b is about 116°C at atmospheric pressure. The reaction section is limited by the thermal degradation of n-pentane at 260°C. The suggested operating pressure ranges between 1.13 and 14.22 atm, so the ARDT evaluated could operate at these conditions. As for ΔT_b , R-DWC, R-HiGee, CCD, and MA-RD could cover those temperature ranges without needing additional units.

- Step 3: hydrogenation of benzene to produce cyclohexane could be accompanied by hydrogenation of toluene into methylcyclohexane (parallel reaction) and isomerisation of cyclohexane into methyl cyclopentane (series reaction) – equations (38) to (40) in the Supplementary Information. Kinetic data are scarce, particularly for the reaction in the liquid phase and the type of catalyst, where the latter is usually kept as a trade secret, according to Mahindrakar and Hahn (2014). Reaction rate values at different temperatures are provided in Table S5.28 in the Supplementary Information. The reaction rate order for the hydrogenation of benzene, which is within the temperature range evaluated in the operating window, fluctuates between 10^{-5} and 10^{-4} , which can be favoured with the use of CCD. Regarding side reactions, reference values are provided, but under conditions outside the range of pressures identified in the operating window. However, Campbell (2011) provided a qualitative reference for the isomerisation reaction, which could be slow enough if temperatures are controlled. Although the side reactions cannot be represented in the operating windows due to the lack of data in the required conditions, identifying the type of reactions could provide guidance to select R-DWC and R-HiGee, since they could help prevent side reactions.
- Step 4: the system exhibits two homogeneous azeotropes (Table S5.29 in the Supplementary Information). The most problematic azeotrope occurs between benzene and cyclohexane, which is pressure sensitive and disappears above two atmospheres. A membrane module could be added to overcome the azeotrope in case benzene is not fully converted and exits the system.

Results of the methodology are summarised in Table 5.12, where R-DWC is ranked as the most advantageous technology, followed by MA-RD and CCD. Additional separation is needed to obtain all the streams. Two additional units – a guard bed reactor and a membrane – are included to deal with sulphur compounds in the feed and the azeotrope between benzene and cyclohexane, respectively. The application in the decision-making flowchart is illustrated in Figure S5.20 in the Supplementary Information.

Table 5.12. Decision-making matrix for the cyclohexane system

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	🟡	🟢	🟡	🟡		🟢		Advantageous (Rank 1)	ii, iii, vi
R-HiGee			🟡	🟡	🔴	🟢		Not applicable	ii, iii, vi
R-HiDiC			🟡	🔴				Not applicable	ii, iii, vi
CCD			🟡	🟡	🟢			Advantageous (Rank 3)	ii, iii, vi
MA-RD	🟡		🟡	🟡			🟢	Advantageous (Rank 2)	ii, iii, vi

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

A potential process flowsheet is presented in Figure 5.13, including potential operations conditions. The guard bed reactor and the membrane module are denoted with dotted lines to indicate that they are optional.

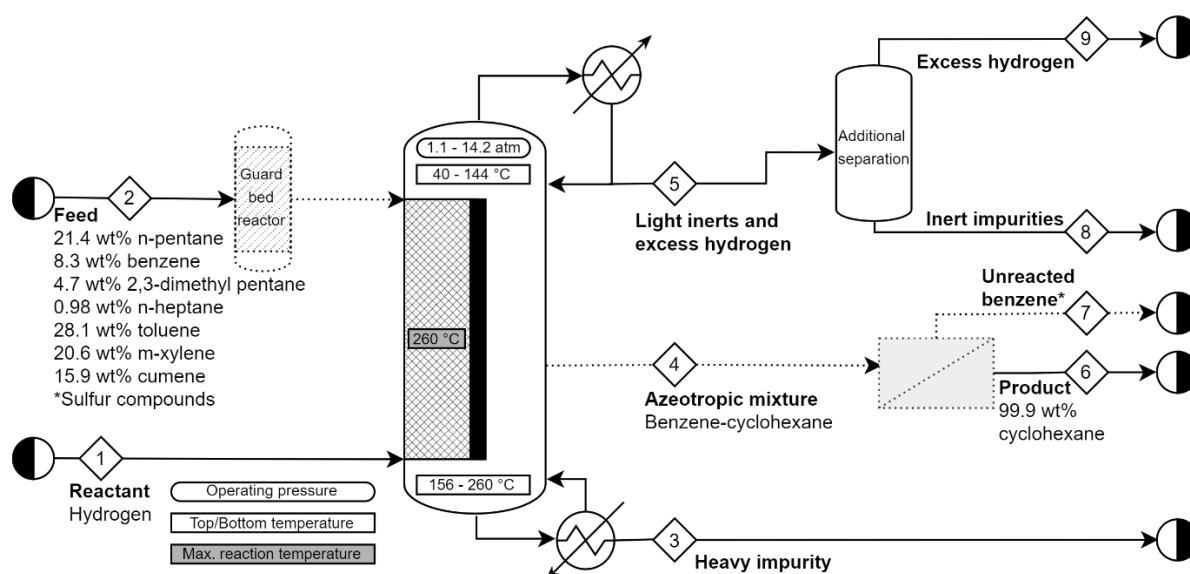


Figure 5.13. PFD for the cyclohexane system for an R-DWC (*Case dependent components. Optional units are denoted with dotted lines)

This case study aimed to demonstrate the application of ARDT in a system where one reactant is a gas that reacts in the liquid phase while in contact with a catalyst. This is important because a range of systems with a gaseous reactant – typically requiring high temperatures and pressures – could be explored and be benefited from simultaneous reaction and separation in RD at less severe conditions. Additionally, this case study demonstrated that a small number of kinetic data points or qualitative information are valuable in providing guidance for the decision-making flowchart, at least at an early stage.

5.2.5.5.3 Comparison of the results of the methodology with the literature

Hydrogenation of benzene in RD is reported in a few studies regarding process control and one patent (Gildert, 2001; Mahindrakar and Hahn, 2016, 2014). However, studies are yet to be performed to evaluate ARDT. While preliminary, having identified R-DWC, MA-RD and CCD

as advantageous provides a good starting point not only for embarking on more rigorous simulations but for identifying additional studies needed to complement the evaluation, particularly regarding kinetics and the type of catalysts.

5.2.6 Conclusions

This work successfully proposed and validated a systematic synthesis methodology to assess ARDT to identify features to qualify them as advantageous, technically feasible, or not applicable. This methodology allows the evaluation of different scenarios to understand the effect of operating conditions, side reactions, dilute feeds and azeotropes, which are typically overlooked in the early stages of process design. The results can be presented in a process flowsheet, including units to complement the operation of ARDT to solve the design problem. Thus, this study strongly contributes to integrating the evaluation of intensified units, whose evaluation is normally unit-oriented, into the process systems engineering approach to obtain an initial process flow diagram.

The methodology was successfully applied and demonstrated in five case studies that are industrially relevant. From a practical point of view, testing different chemical systems demonstrates the robustness and flexibility of the methodology to provide a basis for the selection of technologies. From a methodological point of view, this is the first time that ARDT are considered in a systematic synthesis methodology using a combination of first principles (thermodynamic properties and kinetic parameters) and heuristics. Results are verified with results from other published studies. The main findings of each case study are:

- Purification of lactic acid: It is a special case where a reactive separating agent is introduced to promote a reversible reaction to overcome a difficult separation. It also demonstrates the effects of a reactive impurity. R-DWC was the most advantageous technology because it favours the removal of various outlet streams, particularly the product cut, and could potentially help prevent side reactions.
- Production of dimethyl ether: CCD is deemed potentially advantageous because of the large residence times provided. However, R-DWC and MA-RD were also identified to be feasible and were also evaluated in published studies. Thus, complementary studies are recommended to allow a more quantitative comparison.
- Production of tert-amyl methyl ether: This case study evaluated the effect of side reactions. While R-HiDiC and MA-RD are identified as equally advantageous when side reactions are not considered, R-DWC offers more advantages when accounting for side

reactions because of the additional outlet streams, the location of the product cut and the need to inhibit undesired reactions. In this manner, the methodology provided guidance for selecting technologies accompanied by insights about the parameters influencing the selection, which could inform further kinetic and catalytic studies.

- Production of methyl acetate: This case study demonstrated the flexibility of the methodology that could be adapted according to the objectives of the design problem. R-DWC was identified as the most favourable technology in all scenarios, but the next best technologies varied based on considerations or assumptions tailored to a particular application.
- Production of cyclohexane: This case study investigated a system that includes a gaseous reactant, where R-DWC was found to be the most advantageous. It is worth noting that additional units are also suggested throughout the decision-making flowchart to complement the operation of ARDT and provide a potential process configuration.

For the case studies evaluated, R-HiGee is either considered not applicable or is ranked after other more advantageous technologies. This could be attributed to the fact that the reaction systems evaluated presented slow to intermediate reaction rates, while R-HiGee is deemed advantageous for very fast reactions (where side reactions must be avoided). Therefore, applications featuring relatively fast reactions could potentially find advantages in the use of R-HiGee.

The proposed synthesis methodology finds limitations when complex feeds and reaction networks increase the number of interdependent interactions that cannot be evaluated. Despite the exploratory nature of the methodology, its guidelines assist the selection of technologies and contribute to the development of basic process flowsheets that include ARDT that have not been considered in previous approaches.

Further research should be carried out to understand the interplay of mass and heat transfer and miscibility gaps in ARDT. These investigations will contribute to the future development of methodologies to assist in process synthesis and design. For example, introducing dimensionless numbers, such as the Damköhler and Hatta numbers, will allow operating parameters and hardware characteristics of ARDT to be considered. In addition, cost estimates, which cannot be done at this stage due to the screening nature of the methodology, could be introduced to provide a quantitative measure for comparison. Opportunities for heat integration could be explored by introducing more complex configurations, such as heat

integration in thermally coupled reactive distillation sequences, in later stages of the (detailed) process design.

Acknowledgement

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5.3 Supplementary Information for Publication 4

The Supplementary Information presents a comprehensive reference for the data used as input for the application of the synthesis methodology.

5.3.1 Case studies: Input data and decision-making flowchart

This section thoroughly details the information required to apply the synthesis methodology for each case study. First, a table provides general characteristics of the system, including details about conventional processing options, main feed and product specifications, comments about relevant thermodynamic properties, main and side reactions and phase equilibria. Then, another table presents numerical values to specify the feed, kinetic parameters for the main and side reactions and the heat of reaction. Another table presents components and azeotropes of the system listed in increasing boiling point order. Finally, the decision-making process is described through the navigation of the flowchart.

5.3.1.1 Purification of lactic acid

An overview of the lactic acid system is provided in Table S5.13, and numerical values relevant for the application in the decision-making flowchart are provided in Table S5.14. Equation (24) presents the main reaction and equations (25) to (28) the side reactions. Table S5.15 details the boiling points and type of azeotropes in the system. Finally,

Figure S5.14 illustrates the application of the decision-making flowchart to guide technology selection.

Table S5.13. Overview of the lactic acid system

Features	Lactic acid
Reaction	Highly dilute lactic acid into purified lactic acid by promoting an esterification reaction with methanol to facilitate esters separation
Conventional operation	Lactic acid is produced by fermentation and then purified using liquid-liquid extraction, distillation, membranes with electrodialysis and anion exchange (Starr and Westhoff, 2014).
Characteristics of the feed and product specifications	Feed stream containing large amounts of water, lactic acid and heavy impurities (e.g., succinic acid) (Su et al., 2013). Product food grade LA 88% wt. (Musashino, 2020)
Basic thermodynamic properties	Boiling point of lactic acid and succinic acid unsuitable for distillation due to risk of reaching thermal degradation
Kinetics and side reactions	Esterification of lactic acid with methanol (Sanz et al., 2004) Side reaction of the impurity (i.e., succinic acid) (Dudáš et al., 2014) and oligomerisation of lactic acid (Asthana et al., 2006)
Phase equilibria	Azeotropes forming between water, esters and acids. No multiple phases.

Table S5.14. Input values for evaluating the lactic acid system

Starting questions and decision points	Information needed	Reference values	Source
Inlet streams and compositions?	Feed stream molar composition	Lactic acid: 0.084 Water: 0.905 Succinic acid: 0.011	Su et al. (2013)
Materials/ methods constraints?	Catalyst type and constraints	Amberlyst 35: Degradation temperature 150°C	Dupont (2019)
	Reactants	Succinic acid degradation temperature value: 235°C	Komesu et al.(2017b)
Reaction rate constant? Esterification of lactic acid	Activation energy (kJ kmol ⁻¹)	48733	Regressed from Sanz et al. (2004)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	2.17E+04	Regressed from Sanz et al. (2004)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	2.12E-03	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	2.09E-02	Calculated
	Heat of reaction (kJ mol ⁻¹)	-16.23	Sanz et al. (2004)
Reaction rate constant? Hydrolysis of methyl lactate	Activation energy (kJ kmol ⁻¹)	48487	Regressed from Sanz et al. (2004)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	1.06E-03	Regressed from Sanz et al. (2004)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	1.12E-10	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	1.10E-09	Calculated
	Heat of reaction (kJ mol ⁻¹)	16.23	Sanz et al. (2004)
Side reactions? Esterification of succinic acid into monomethyl succinate	Activation energy (kJ kmol ⁻¹)	78646	Dudáš et al. (2014)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	4.40E+07	Dudáš et al. (2014)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	2.14E-04	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	8.62E-03	Calculated
	Heat of reaction (kJ mol ⁻¹)	-13.43	Calculated from heats of formation in the liquid phase in DIPPR (2021)
Side reactions? Oligomerisation of lactic acid	Activation energy (kJ kmol ⁻¹)	52000	Ashtana et al. (2006)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	20	Ashtana et al. (2006)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	6.63E-07	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	7.62E-06	Calculated
	Heat of reaction (kJ mol ⁻¹)	-	Not available

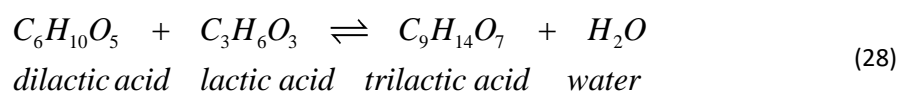
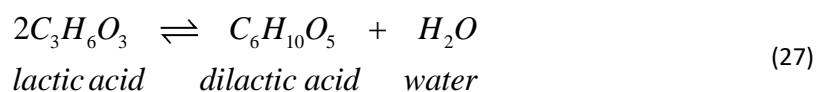
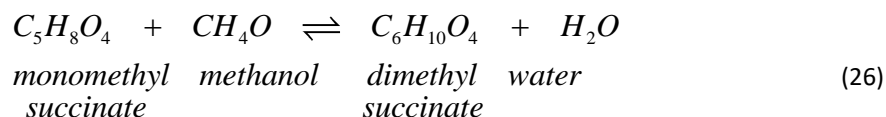
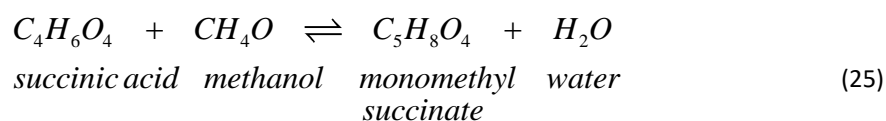
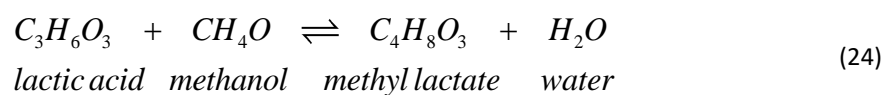


Table S5.15. NBP of pure components and azeotropes in the lactic acid system

Component/Azeotrope	NBP (°C)	Type of azeotrope
Methanol	64.5	-
Water-Dimethyl succinate	98.9	Homogeneous
Water-Methyl lactate	99.9	Homogeneous
Water	100.0	-
Methyl lactate	144.8	-
Lactic acid-Dimethyl succinate	192.8	Homogeneous
Dilactic acid-Dimethyl succinate	193.6	Homogeneous
Dimethyl succinate	196.4	-
Dilactic acid	215.9	-
Lactic acid-Monomethyl succinate	216.4	Homogeneous
Lactic acid	216.6	-
Monomethyl succinate	222.7	-
Succinic acid	317.6	-
Trilactic acid	345.9	-

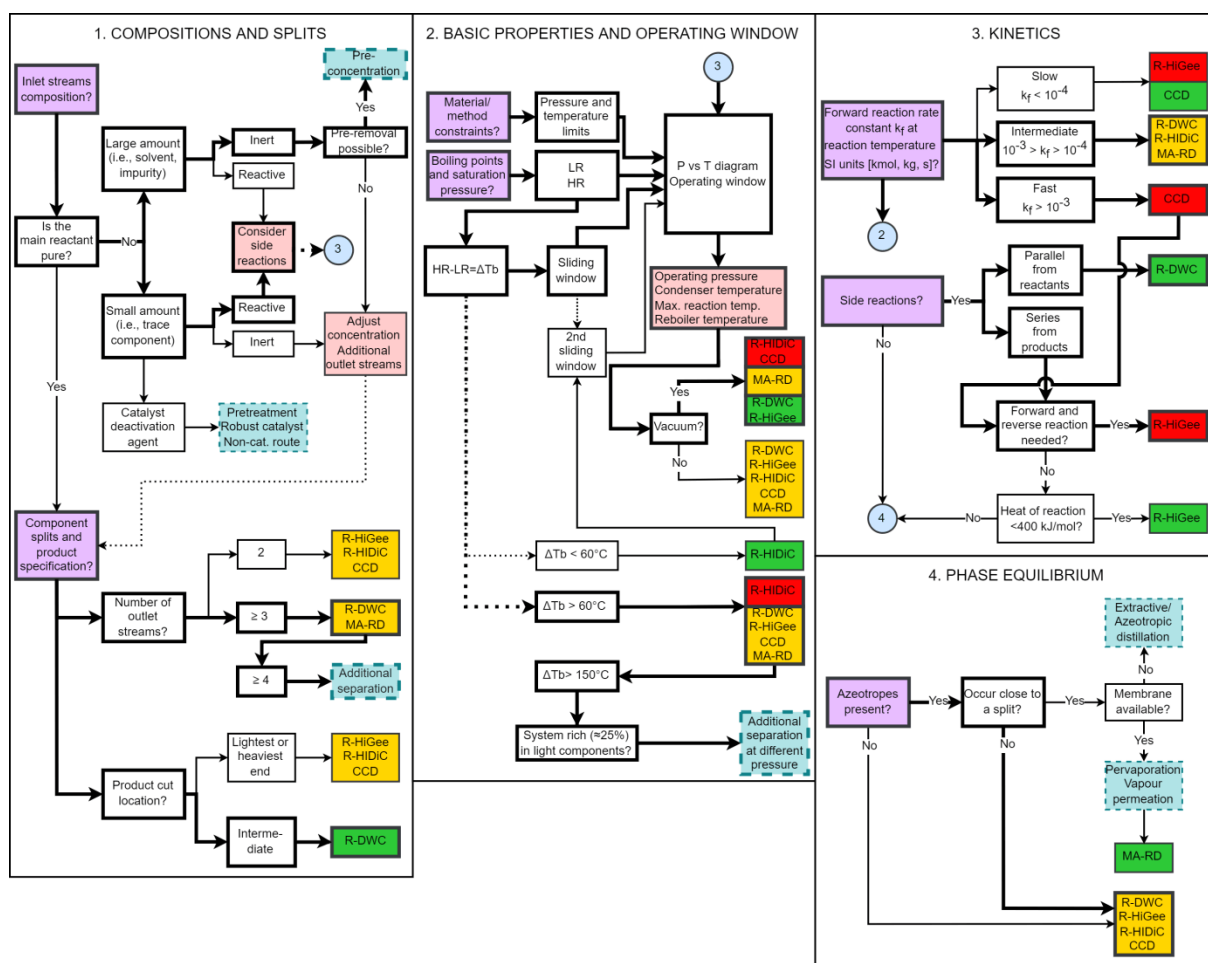


Figure S5.14. Decision-making process for the purification of lactic acid

5.3.1.2 Production of dimethyl ether (DME)

An overview of the DME system is provided in Table S5.16, and numerical values relevant to the application in the decision-making flowchart are provided in Table S5.17. Dehydration of methanol is presented in equation (29). Finally, Figure S5.15 illustrates the application of the decision-making flowchart to guide technology selection.

Table S5.16. Overview of the DME system

Features	Dimethyl ether
Reaction	Methanol to produce DME and water
Conventional operation	Gas-phase reaction in a catalytic fix-bed reactor. Typical conditions are 250°C to 400°C and operating pressure up to 20 bar (Müller and Hübsch, 2000).
Characteristics of the feed and product specifications	Feed stream uses pure methanol (Kiss and Suszwalak, 2012) DME is produced at 99.95% wt. technical grade and 99.99% wt. high-purity (Müller and Hübsch, 2000).
Basic thermodynamic properties	DME presents high vapour pressure, which requires the use of pressure above atmospheric conditions
Kinetics and side reactions	Equilibrium-limited reaction for the dehydration of methanol (Lei et al., 2011), with water as the only byproduct No side reactions (Di Stanislao et al., 2007)
Phase equilibria	No azeotropes present in the system Two liquid phases form when the mixture is rich in water and lean in methanol (Park et al., 2007).

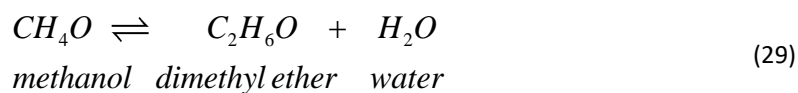


Table S5.17. Input values for the production of DME

Starting questions and decision points	Information needed	Reference values	Source
Inlet streams and compositions?	Feed stream molar composition	Pure methanol	Kiss and Suszwalak (2012)
Materials/ methods constraints?	Catalyst type and constraints	Amberlyst 35: Degrad. temp. 150°C	Dupont (2019)
	Reactants	-	-
Reaction rate constant? Dehydration of methanol	Activation energy (kJ kmol ⁻¹)	133800	Original data Lei et al. (2011) given per unit volume of liquid. Assuming a liquid molar density of 0.0375 kmol/m ³ and that the molar composition of the mixture is 0.2 (DME), 0.4 (methanol) and 0.4 (water)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	1.95E+08	
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	1.10E-11	Calculated
	Forward reaction rate constant at max.reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	5.92E-09	Calculated
	Heat of reaction (kJ mol ⁻¹)	-25.56	Kasaie and Sohrabi (2009)

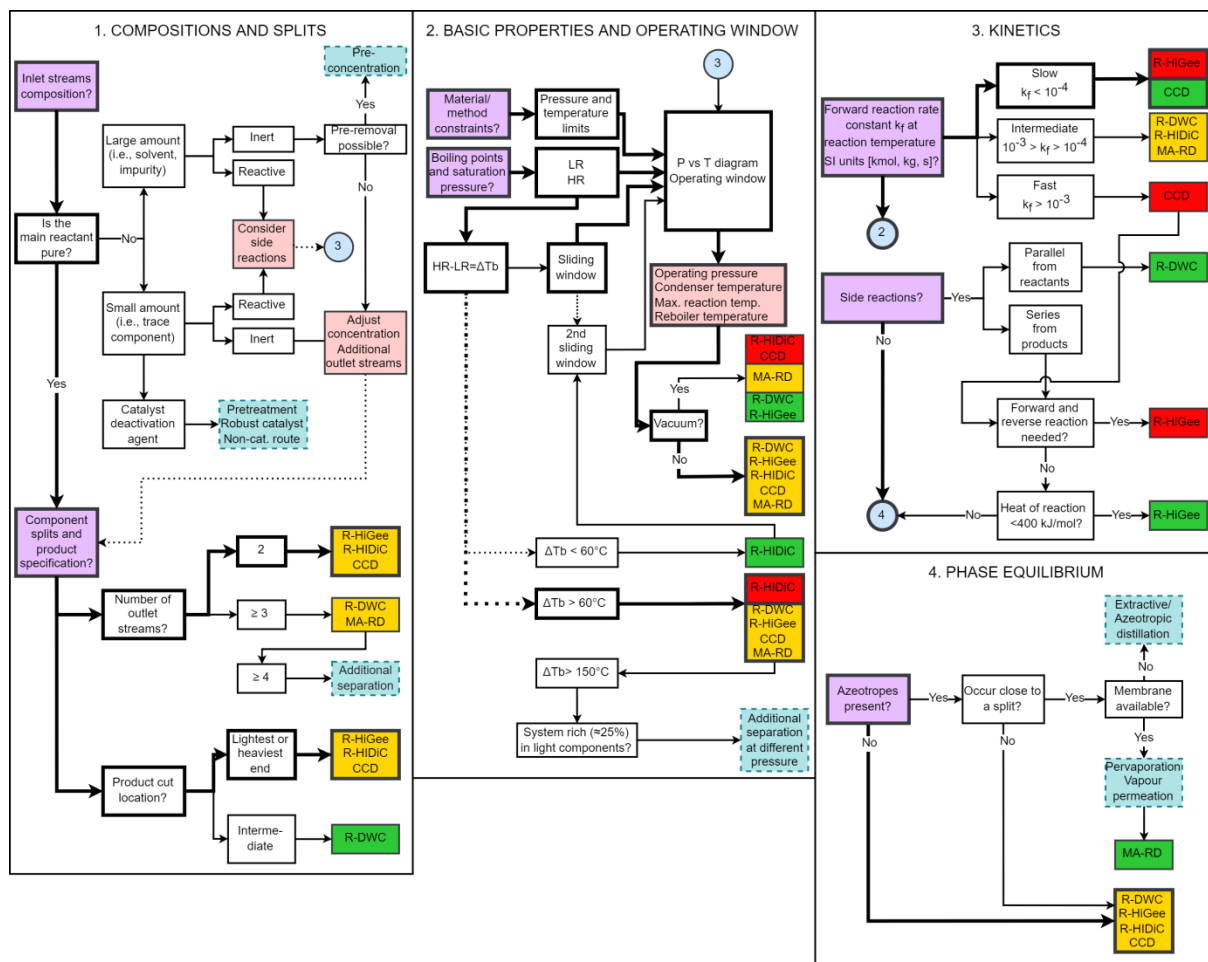


Figure S5.15. Decision-making process for the production of DME

5.3.1.3 Production of tert-amyl methyl ether

An overview of the TAME system is provided in Table S5.18 and the input values used to apply the synthesis methodology in both Scenario 1 and Scenario 2 are presented in Table S5.19.

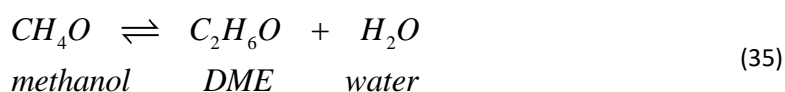
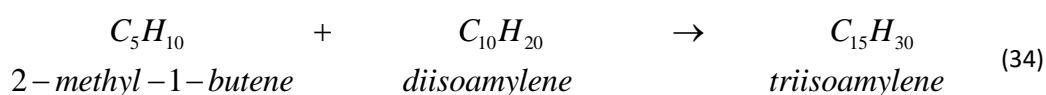
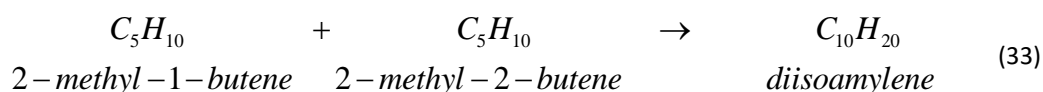
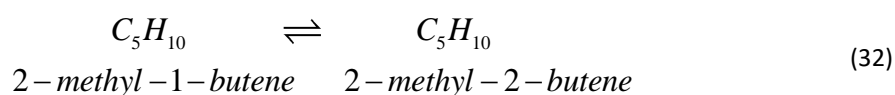
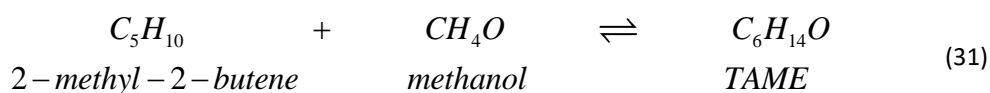
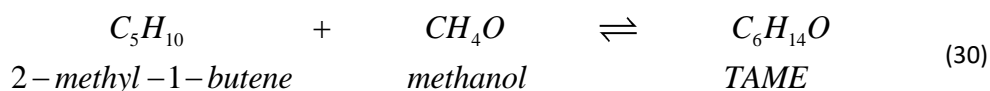
Table S5.18. Overview of the TAME system

Features	Tert-amyl methyl ether
Reaction	Addition of isoamylenes to methanol to produce TAME
Conventional operation	Two reactors and a methanol recovery unit (Marcilly, 2005)
Characteristics of the feed and product specifications	Feed stream produced in the FFC unit, containing isoamylenes and mixed C5 components (Boz and Dogu, 2005; Subawalla and Fair, 1999) Product purity larger than 98% mol
Basic thermodynamic properties	All components are relatively close boiling with a temperature difference between the lightest and heaviest from 60 to 70°C approximately depending on the selected operating pressure
Kinetics and side reactions	Main equilibrium-limited reactions: two reactions that produce TAME from isoamylenes, and one isomerisation reaction between 2M1B and 2M2B (Luyben and Yu, 2008) Possible side reactions include the formation of dimers and trimers of 2M1B and 2M2B (Cruz et al., 2007), methanol condensation to dimethyl ether (Lei et al., 2011), and isoamylenes hydration to tert-amyl alcohol (TAA) when water is present (Subawalla and Fair, 1999).
Phase equilibria	All the C5 components form minimum-boiling azeotropes with methanol and contribute significantly to the nonideality of the reaction mixture (Subawalla and Fair, 1999).

Table S5.19. Input values for the production of TAME system

Starting questions and decision points	Information needed	Reference values	Source
Inlet streams and compositions?	Feed stream molar composition	Isopentane (i): 0.482 1-pentene (i):0.036 2-methyl-1-butene: 0.082 2-methyl-2-butene: 0.159 Cyclopentane (i): 0.241	Adapted from Subawalla and Fair (1999)
Materials/ methods constraints?	Catalyst type and constraints	Amberlyst 35: Degradation temperature 150°C	Dupont (2019)
Reaction rate constant? Main reactions	Activation energy (kJ kmol ⁻¹)	(30): 76103.7 (31): 98230.2 (32): 96522.6	Luyben and Yu (2008)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	(30): 1.33E+08 (31): 1.37E+11 (32): 2.72E+10	Luyben and Yu (2008)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	(30): 1.50E-03 (31): 1.02E-03 (32): 3.56E-04	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	(30): 5.35E-02 (31): 1.03E-01 (32): 3.31E-02	Calculated
	Heat of reaction (kJ mol ⁻¹)	(30): -34.44 (31): -26.76 (32): -7.67	Luyben and Yu (2008)
Side reactions? Dimerisation to 2,3,4,4-tetramethyl-1-hexene	Activation energy (kJ kmol ⁻¹)	50422.7	Cruz et al. (2007)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	5612.8	Cruz et al. (2007)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	3.11E-04	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	3.33E-03	Calculated
	Heat of reaction (kJ mol ⁻¹)	-67.23	Calculated
Side reactions? Trimerisation to 2,4,6,6,7,7-hexamethylnon-3-ene	Activation energy (kJ kmol ⁻¹)	62025.4	Cruz et al. (2007)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	1.61E+06	Cruz et al. (2007)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	1.92E-03	Calculated
	Forward reaction rate constant at max.reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	3.53E-02	Calculated
	Heat of reaction (kJ mol ⁻¹)	-69.58	Calculated
Side reactions? Dehydration of methanol	Activation energy (kJ kmol ⁻¹)	1.34E+05	Lei et al. (2011)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	1.95E+08	Lei et al. (2011)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	1.10E-11	Calculated
	Forward reaction rate constant at max. reaction temp. (150°C) (kmol kg ⁻¹ s ⁻¹)	5.92E-09	Calculated
	Heat of reaction (kJ mol ⁻¹)	-25.56	Kasaie and Sohrabi (2009)

The main reactions of the system evaluated in Scenario 1 are equations (30) to (32), whereas the side reactions included in Scenario 2 are presented in equations (33) to (35).



The azeotropes appearing in Scenario 1 and Scenario 2 are presented in Table S5.20 and Table S5.21, respectively.

Table S5.20. NBP of pure components and azeotropes in the TAME system (Scenario 1)

Component/Azeotrope	NBP (°C)	Type of azeotrope
Methanol-Isopentane	25.05	Heterogeneous
Methanol-1-pentene	27.45	Heterogeneous
Methanol-2M1B	27.82	Heterogeneous
Isopentane	27.85	—
Isopentane-1-pentene	27.85	Homogeneous
1-pentene	30.05	—
2M1B	31.15	—
Methanol-2M2B	33.19	Heterogeneous
2M2B	38.5	—
Methanol-Cyclopentane	43.64	Homogeneous
Cyclopentane	49.27	—
Methanol-TAME	62.19	Homogeneous
Methanol	64.53	—
TAME	86.28	—

Table S5.21. NBP of pure components and azeotropes in the TAME system (Scenario 2)

Component/Azeotrope	NBP (°C)	Type of azeotrope
Dimethyl ether	-24.78	–
Methanol-Isopentane	25.05	Heterogeneous
Isopentane-1-pentene-water	26.84	Heterogeneous
Isopentane-water	26.84	Heterogeneous
Methanol-1-pentene-water	27.38	Heterogeneous
Methanol-1-pentene	27.45	Heterogeneous
Methanol-2M1B	27.82	Heterogeneous
Isopentane	27.85	–
Isopentane-1-pentene	27.85	Homogeneous
1-pentene-water	28.9	Heterogeneous
1-pentene	30.05	–
2M1B-water	30.51	Heterogeneous
2M1B	31.15	–
Methanol-2M2B	33.19	Heterogeneous
2M2B-water	36.73	Heterogeneous
2M2B	38.5	–
Methanol-cyclopentane-water	43.09	Heterogeneous
Methanol-cyclopentane	43.64	Homogeneous
Cyclopentane-water	46.12	Heterogeneous
Cyclopentane	49.27	–
Methanol-TAME	62.19	–
Methanol	64.53	–
TAME-water	73.87	Heterogeneous
TAME	86.28	–
Dimer-water	99.28	Homogeneous
Water	100.02	–
Dimer	123.79	–
Trimer	219.84	–

Finally, the path followed in the decision-making flowchart is illustrated in Figure S5.16 for Scenario 1 and in Figure S5.17 for Scenario 2.

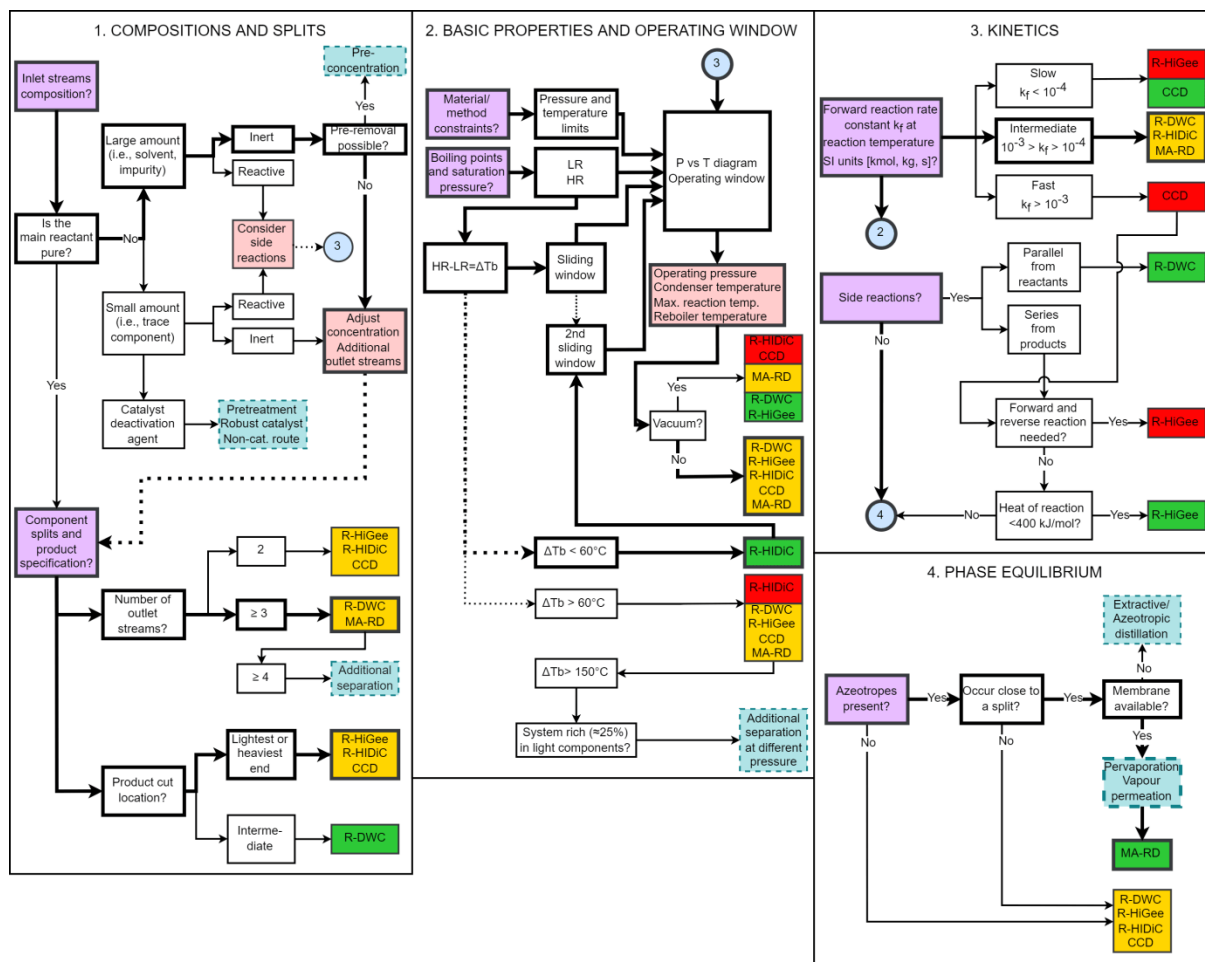


Figure S5.16. Decision-making process for the production of TAME (Scenario 1)

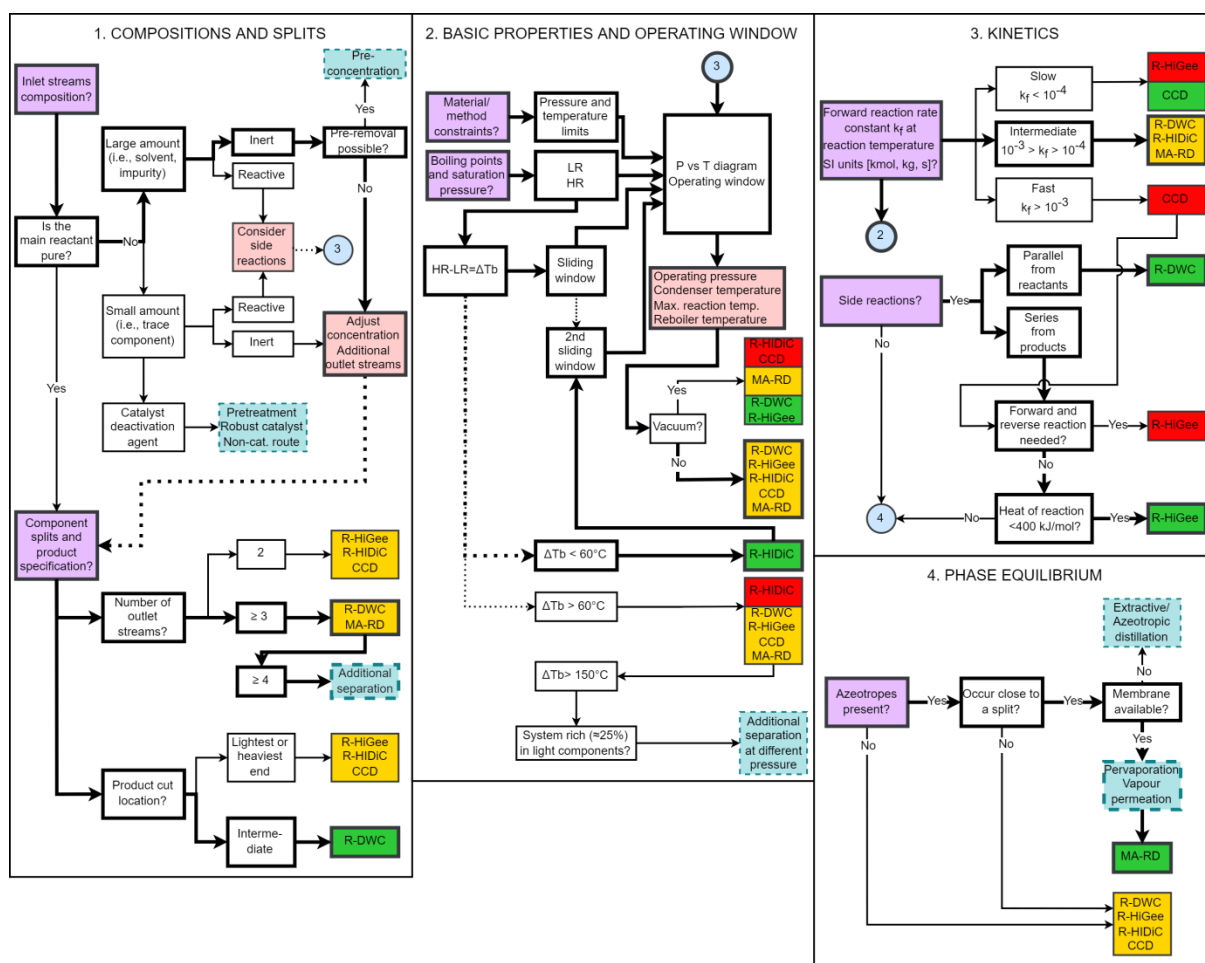


Figure S5.17: Decision-making process for the production of TAME (Scenario 2)

5.3.1.4 Production of methyl acetate

A general overview of the methyl acetate system is presented in Table S5.22 and numerical values used in the decision-making methodology are presented in Table S5.23.

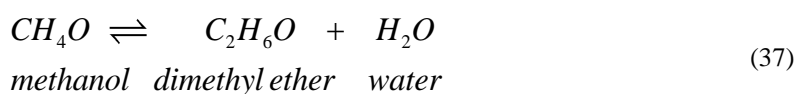
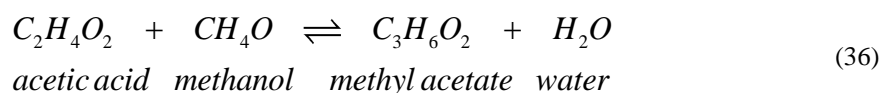
Table S5.22: Overview of the methyl acetate system

Features	Methyl acetate
Reaction	Esterification reaction of acetic acid with methanol to produce methyl acetate and water
Conventional operation	Most methyl acetate is a byproduct of the production of acetic acid. Another method is the esterification of acetic acid with methanol. A ground-breaking technology is the use of reactive distillation that replaced a process containing several unit operations (Berre et al., 2014).
Characteristics of the feed and product specifications	The feed streams used are typically high-purity acetic acid and methanol (An et al., 2015; Pöpken et al., 2001) Methyl acetate is commercialised in different compositions ranging from 95% wt. to 99.5% wt. (Eastman, 2022)
Basic thermodynamic properties	Methyl acetate is the most volatile ester, and the lightest component of the system.
Kinetics and side reactions	Equilibrium-limited reaction of methanol and acetic acid (Pöpken et al., 2001) Potential dehydration of methanol to produce dimethyl ether
Phase equilibria	The system features two azeotropes: methanol-methyl acetate and water-methyl acetate. There is also a miscibility gap occurring at low concentrations of methanol and high concentrations of methyl acetate and water.

Table S5.23. Input values for the production of methyl acetate system

Starting questions and decision points	Information needed	Reference values	Source
Inlet streams and compositions?	Feed stream molar composition	Pure methanol	An et al. (2015)
	Feed stream molar composition	Pure acetic acid	An et al. (2015)
Materials/ methods constraints?	Catalyst type and constraints	Amberlyst 15 Degradation temperature: 120°C	Pöpken et al. (2000)
	Reactants	NA	-
Reaction rate constant? Esterification of acetic acid	Activation energy (kJ kmol ⁻¹)	49190	Pöpken et al. (2000)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	2.96E+04	Pöpken et al. (2000)
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	2.49E-03	Calculated
	Forward reaction rate constant at maximum reaction temperature (120°C) (kmol kg ⁻¹ s ⁻¹)	8.63E-03	Calculated
	Heat of reaction (kJ mol ⁻¹)	4.328	Mekala and Goli (2015)
Reaction rate constant? Dehydration of methanol	Activation energy (kJ kmol ⁻¹)	133800	Original data Lei et al. (2011) given per unit volume of liquid. Assuming a liquid molar density of 0.0375 kmol/m ³ and a molar composition of 0.2 (DME), 0.4 (methanol) and 0.4 (water)
	Pre-exponential factor (kmol kg ⁻¹ s ⁻¹)	1.95E+08	
	Forward reaction rate constant at 90°C (kmol kg ⁻¹ s ⁻¹)	1.10E-11	Calculated
	Forward reaction rate constant at maximum reaction temperature (120°C) (kmol kg ⁻¹ s ⁻¹)	5.92E-09	Calculated
	Heat of reaction (kJ mol ⁻¹)	-25.56	Kasaie and Sohrabi (2009)

Esterification of acetic acid is presented in equation (36) and the potential side reaction for dehydration of methanol is shown in equation (37).



The list of azeotropes and their boiling points are presented in Table S5.24. The decision-making flowchart and the path followed to aid technology selection is presented in Figure S5.18.

Table S5.24: NBP of pure components and azeotropes in the methyl acetate system

Components	NBP (°C)	Type of azeotrope
DME	-24.78	-
Methanol-methyl acetate	53.57	Homogeneous
Water-methyl acetate	56.98	Homogeneous
Methyl acetate	57.05	-
Methanol	64.53	-
Water	100.02	-
Acetic acid	118.01	-

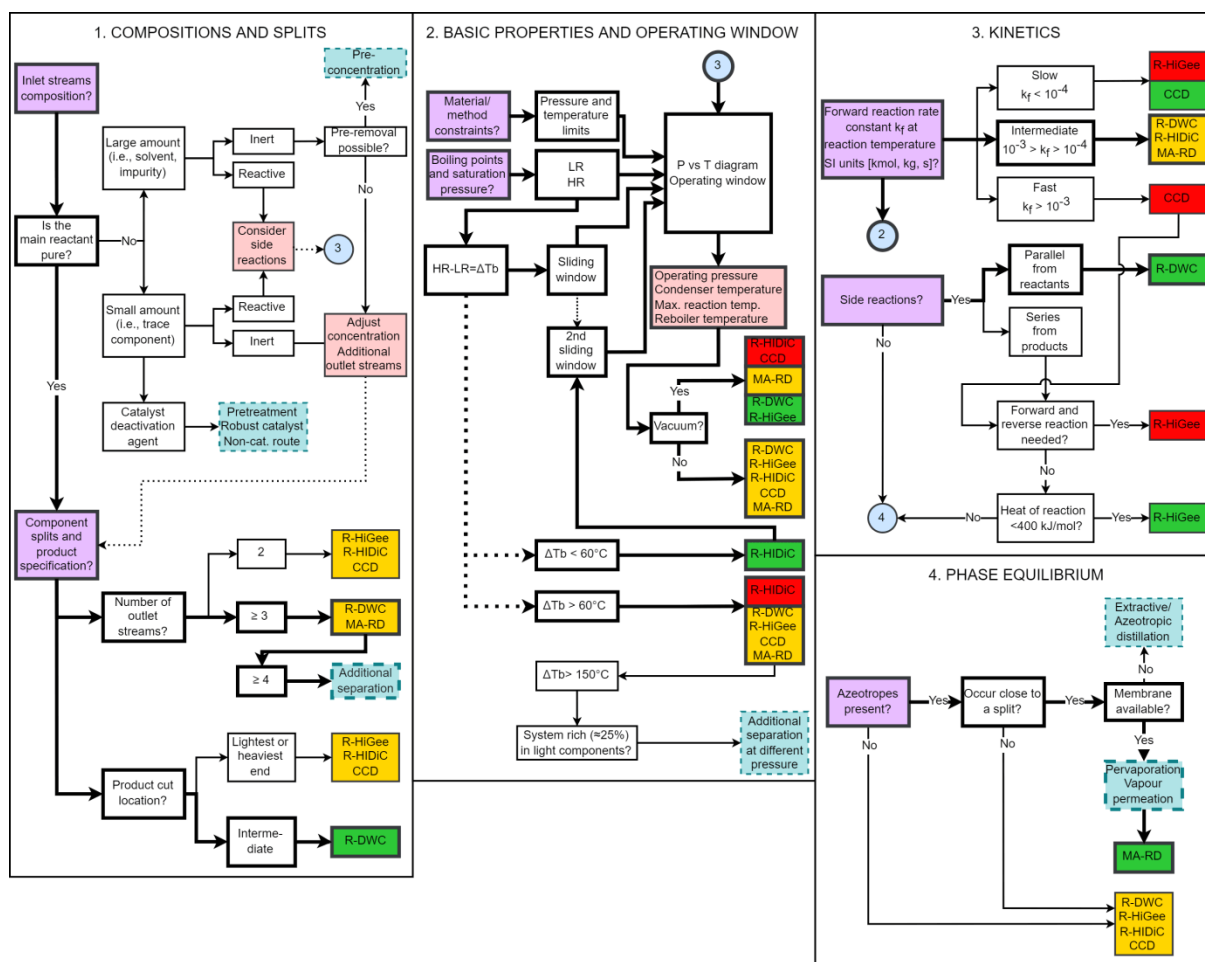


Figure S5.18. Decision-making process for the production of methyl acetate

5.3.1.4.1 Hydrolysis of methyl acetate

The reverse reaction for the methyl acetate case was evaluated to identify which decision points derive in a different suggestion for technology selection.

- Step 1: Table S5.25 lists the components participating in the hydrolysis of methyl acetate. DME does not appear as a byproduct. However, the nature of the component changes as methyl acetate is now a reactant and the main product is acetic acid. Assuming that water is fed in excess, three outlet streams are expected. The product is the heaviest species, which is removed from the bottom.

Table S5.25. List of components, nature and splits for methyl acetate hydrolysis

Components	Nature	NBP (°C)	Output stream
Methyl acetate	Reactant	56.9	–
Methanol	Byproduct	64.7	1
Water	Reactant	100.0	2
Acetic acid	Product	117.9	3

- Step 2: the boiling point order and the representative components remain the same, hence the operating window and the corresponding operating conditions will not change and the results from step two do not differ compared to the esterification.
- Step 3: the hydrolysis reaction rate constant is one order of magnitude smaller than the esterification reaction. Nevertheless, it still lies among the intermediate rate range. As no side reactions occur, no guidance emerges from this criterion.
- Step 4: when analysing the azeotrope data (Table S5.24), the azeotrope still exists but it is not problematic as it is not located near the product, and it is likely to be consumed within the system if methyl acetate is the limiting reactant.

Table S5.26 summarises the results of the synthesis methodology for the hydrolysis of methyl acetate. R-HIDiC is found to be advantageous, which agrees with the studies found in the literature (Chen et al., 2020; Lee et al., 2010; Li et al., 2015; Zhai et al., 2015). Figure S5.19 illustrates the path followed in the decision-making flowchart.

Table S5.26. Decision-making matrix for the hydrolysis of methyl acetate

Criteria	Number of outlet streams	Product cut location	Vacuum operation	ΔT_b	Reaction rate constant	Side reactions	Azeotropes	ARDT selection from the synthesis methodology	Additional technology
R-DWC	!		!		!	-	!	Feasible	iii, vi
R-HiGee		!	!		!	-	!	Feasible	iii, vi
R-HiDiC		!	!	✓	!	-	!	Advantageous	iii, vi
CCD		!	!		!	-	!	Feasible	iii, vi
MA-RD	!		!		!	-		Feasible	iii

i) Preconcentration, ii) Catalyst safeguarding technologies, iii) Additional separation for extra streams, iv) Additional separation at different pressure, v) Azeotrope-oriented technologies, vi) Membrane module

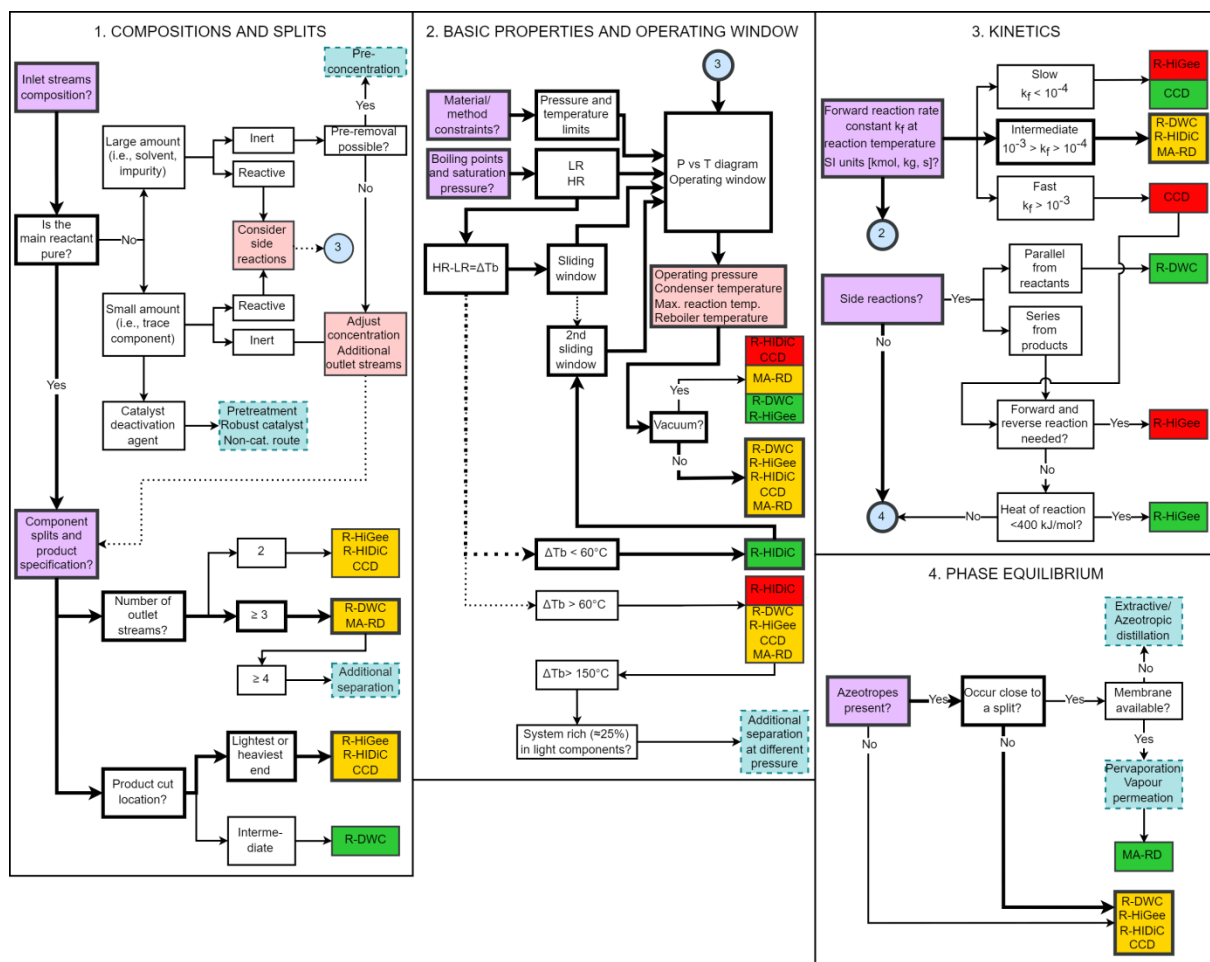


Figure S5.19. Decision-making process for the hydrolysis of methyl acetate

5.3.1.5 Production of cyclohexane

An overview of the cyclohexane system is provided in Table S5.27 and input values used for the synthesis methodology are provided in Table S5.28.

Table S5.27. Overview of the cyclohexane system

Features	Cyclohexane
Reaction	Benzene hydrogenation to produce cyclohexane
Conventional operation	Vapour-phase process with multi-stage reactors in series Liquid-phase reactor (slurry) and vapour-phase reactors (Campbell, 2011)
Characteristics of the feed and product specifications	Feed stream contains benzene, paraffins ranging from C5 to C9, and other aromatics such as toluene, m-xylene and cumene. The benzene content is highly variable between 3 to 11 vol% (Mahindrakar and Hahn, 2014). Hydrogen stream may contain impurities (e.g., CO and light hydrocarbons) depending on the source (Sanderson et al., 2004) Cyclohexane purity is 99.9% wt. (Campbell, 2011)
Basic thermodynamic properties	Hydrogen features a high vapour pressure, and its boiling point is very distant from the other components of the system.
Kinetics and side reactions	Kinetic hydrogenation reaction (Sharma et al., 2011) Potential side reaction between toluene and hydrogen (Mahindrakar and Hahn, 2016) Isomerisation of cyclohexane into methyl cyclopentane formation (Gildert, 2001; Sanderson et al., 2004)
Phase equilibria	Cyclohexane and benzene feature a homogeneous azeotrope at pressures close to atmospheric. At pressures above 2 atm, the cyclohexane-benzene azeotrope disappears (Campbell, 2011)

Table S5.28. Input values for the cyclohexane system

Starting questions and decision points	Information needed	Reference values	Source
Inlet streams and compositions?	Feed stream mass composition Benzene stream	n-pentane: 0.214 benzene: 0.083 2,3-dimethyl pentane: 0.047 n-heptane: 0.0098 Toluene: 0.281 m-xylene: 0.206 Cumene: 0.159	Modified from Mahindrakar and Hahn, (2014)
	Feed stream mass composition Hydrogen stream	Hydrogen: 0.85 Carbon monoxide: <0.05 Light hydrocarbons: <0.10	Sanderson et al. (2004)
Materials/ methods constraints?	Catalyst type and constraints	Ruthenium containing hydrotalcite Degradation temperature: 280°C	Sharma et al. (2011)
	Reactants	n-heptane Degradation temperature: 260°C	Dai et al. (2016)
Reaction rate constant? Hydrogenation of benzene	Initial reaction rate (kmol kg ⁻¹ s ⁻¹)	At 80°C: 4.58E-05 At 110°C: 1.17E-04 At 140°C: 2.08E-04	Sharma et al. (2011)
	Heat of reaction (kJ/mol)	-216.37	Campbell (2011)
Side reactions? Toluene hydrogenation	Reaction rate at 20 bar (kmol kg ⁻¹ s ⁻¹)	At 95°C: 9.72E-6 At 125°C: 1.85E-5 At 140°C: 2.76E-5	Toppinen et al. (1996)
	Heat of reaction (kJ/mol)	-205	Dong et al. (2021)
Side reactions? Isomerisation of cyclohexane	Activation energy (kJ/kmol)	20.2	Triwahyono et al. (2006)
	Pre-exponential factor	Not available	-
	Heat of reaction (kJ/mol)	16.79±2.09	Stevenson and Morgan (1948)

Equation (38) represents the main reaction, while hydrogenation of toluene (39) is a parallel reaction and the isomerisation of cyclohexane (40) is a series reaction.

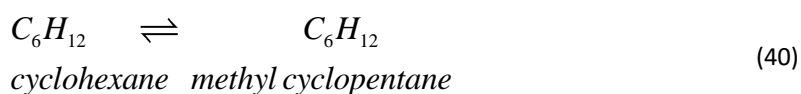
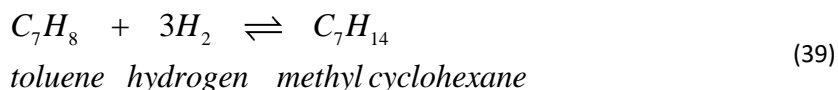
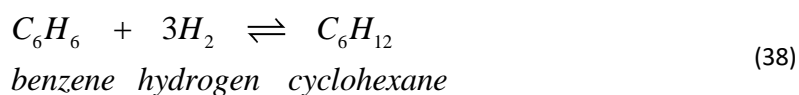


Table S5.29. NBP of pure components and azeotropes in the cyclohexane system

Components	NBP (°C)	Type of azeotrope
Hydrogen	-245.27	—
n-pentane	36.3	—
Methyl cyclopentane	71.49	—
Benzene-2,3-dimethyl pentane	79.99	Homogeneous (disappears above 19 atm)
Benzene-Cyclohexane	80.11	Homogeneous (disappears above 2 atm)
Benzene	80.15	—
Cyclohexane	81.4	—
2,3-dimethyl pentane	89.82	—
n-heptane	98.42	—
Methyl cyclohexane	100.9	—
Toluene	112.15	—
m-xylene	139.16	—
Cumene	152.47	—

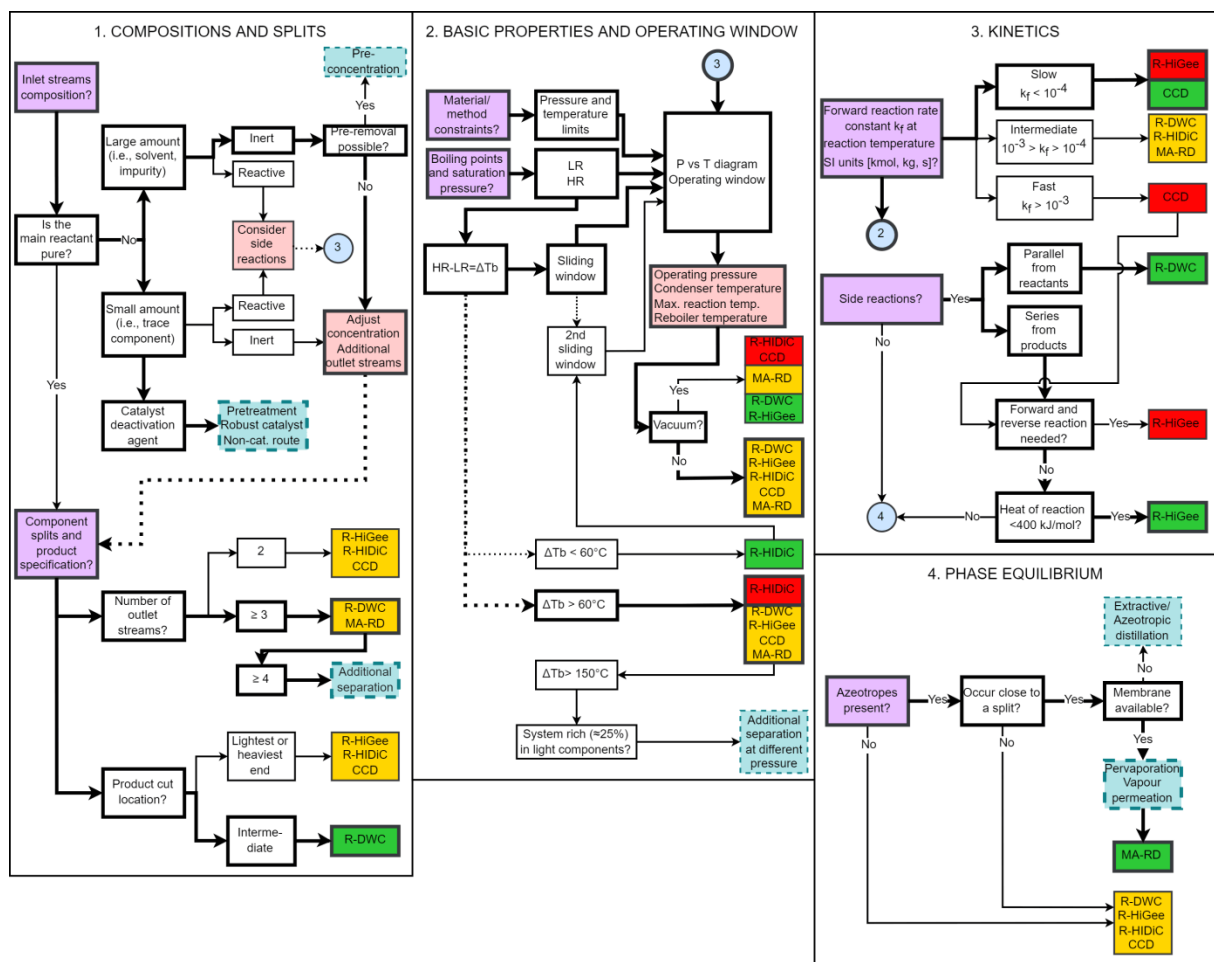


Figure S5.20. Decision-making process for the production of cyclohexane

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Chapter 6

Overview, conclusions and recommendations for future work

6.1 Overview

This PhD thesis presents a systematic methodology to enable quick early-stage assessment of the technical feasibility of advanced reactive distillation technologies (using first principles and heuristics based on thermodynamic properties and kinetic parameters) with less computational effort than mathematical programming-based approaches. The technologies in scope are reactive dividing-wall columns (R-DWC), catalytic cyclic distillation (CCD), reactive internally heat-integrated distillation (R-HiDiC), reactive high-gravity distillation (R-HiGee), and membrane-assisted reactive distillation (MA-RD).

This research used problem-based analyses of case studies in the research literature and detailed process simulation to gain understanding of the subject area and formulate an approach to carry out process synthesis of novel flowsheets. Figure 6.1 provides an overview of this research. The research outputs, highlighted in bold boxes, captured insights for both formulating the research approach and developing the synthesis methodology tailored to the specific research questions and objectives of the study.

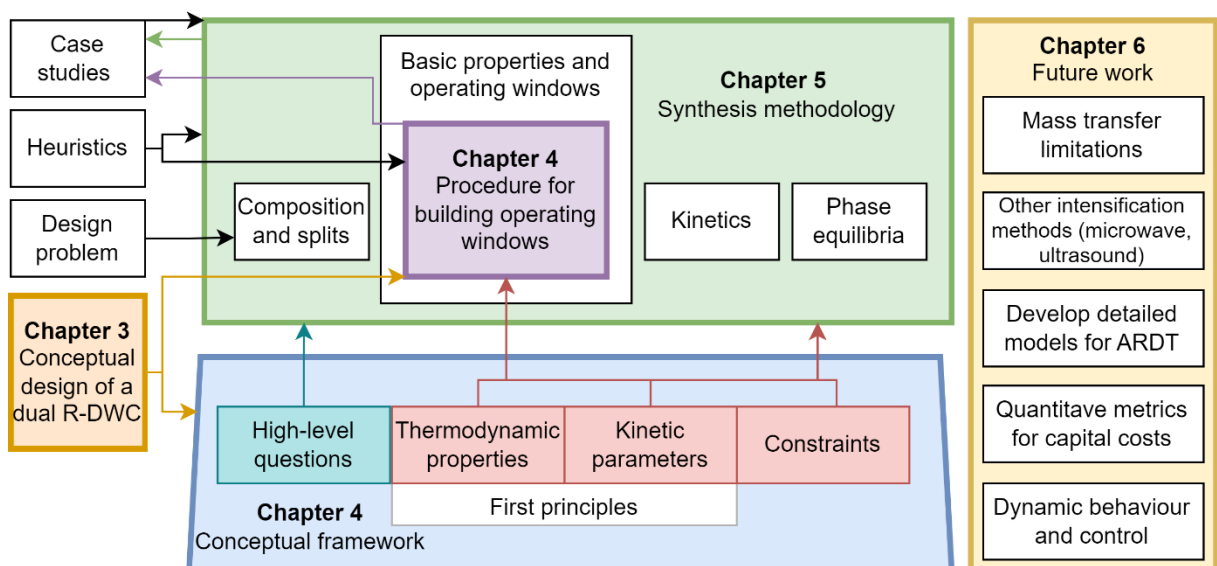


Figure 6.1. Overview of the research

The selected case studies focused on complex chemical systems that were processed using novel technologies. The case studies were chosen to explore and gain insights into the associated characteristics, challenges, and opportunities. The effectiveness of the synthesis methodology was evaluated by comparing the solutions identified as potentially advantageous with flowsheets reported in the research literature, where the latter were synthesised using ad hoc approaches. This systematic methodology represents a significant contribution to the state of the art in this field, as it provides structured guidance for determining whether advanced reactive distillation technologies are potentially beneficial, reduces the amount of required data, and minimises the time spent on design or simulation.

The aim of this PhD thesis, presented in Chapter 1, has been achieved with the development of a systematic methodology to expand the applicability of reactive distillation in terms of operating conditions or the type of chemical systems to which it can be applied by simultaneously assessing the technical feasibility of five advanced reactive distillation technologies and providing insights on their advantages and disadvantages that facilitate visualising trade-offs for technology selection during process synthesis, while minimising requirements for process data and computational effort.

The objectives of this PhD thesis have been met as follows:

Objective 1: The strategies used for the conceptual design of advanced reactive distillation technologies based on published studies were identified by examining the limitations of technology-oriented process design.

- This work, presented in Chapter 2, was used to identify the research gaps and the need for a systematic methodology to conduct the initial assessment of the feasibility of advanced reactive distillation technologies.

Objective 2: A rigorous conceptual design of a dual R-DWC was developed to identify data, interdependent phenomena and constraints that needed to be incorporated into a generalised approach applicable to the synthesis of advanced reactive distillation technologies.

- Chapter 3 presented the conceptual design of a dual reactive dividing wall column applied to purify lactic acid from a fermentation broth characterised by high dilution and the presence of a reactive impurity, succinic acid. The conceptual design using shortcut models and rigorous models in Aspen Plus helped illustrate how challenging and

complex the conceptual process design of reactive distillation technologies is. The resulting flowsheet adapted from previous configurations containing a sequence of reactive distillation and conventional distillation included a flash separator, a dual-reactive dividing wall column and a methanol recovery distillation column. The proposed configuration performed better than sequences relying on reactive distillation and conventional distillation by reducing energy consumption (13–27 %), material intensity (28–32 %), and water consumption (22–36 %), while effectively removing the reactive impurity. These results demonstrated that a dual-reactive dividing wall column could potentially outperform its conventional counterparts in this case.

Objective 3: Basic thermodynamic properties and kinetic parameters were identified, and high-level questions were formulated to define the scope, limitations and data required for the synthesis of advanced reactive distillation technologies using the conceptual design of a dual R-DWC and case studies reported in the literature.

- Chapter 4 presents a conceptual framework and a procedure for building operating windows applicable to advanced reactive distillation technologies. The conceptual framework identifies relevant thermodynamic properties and kinetic parameters and formulates high-level questions to provide insights for the selection of technologies. A subset of high-level questions that provides decision points was applied to two case studies: purification of lactic acid and production of dimethyl ether. Preliminary results from applying these high-level questions suggested that R-DWC is suitable for the purification of lactic acid because of the number of outlet streams required, the byproducts from the side reaction and azeotropes with intermediate boiling temperatures. CCD was deemed suitable for dimethyl ether production due to large holdups that suit a relatively slow reaction. R-DWC could be used to purify the outlet streams.

Objective 4: The concept of operating windows was extended to identify and represent potential interactions between advanced reactive distillation technologies and chemical systems.

- The procedure for building operating windows in Chapter 4 provided simplification strategies to represent multicomponent systems and add flexibility to the location of the windows' boundaries. In particular, two new concepts are proposed: 'representative components' and 'sliding windows'. The application of the proposed procedure is

demonstrated in three case studies: the production of methyl acetate, purification of lactic acid, and production of tert-amyl methyl ether. Thus potential ranges of operating conditions were identified using basic data, and complex features, such as multicomponent feeds and side reactions, were successfully represented in an operating window. These results suggest that the impact of complex features on the design of advanced reactive distillation technologies could be determined early on.

Objective 5: Using first principles and heuristics, a synthesis methodology was established to qualitatively evaluate the advantages and disadvantages of advanced reactive distillation technologies applied to a chemical system to provide insights for the development of basic process flowsheets.

- Chapter 5 presented a systematic methodology for the synthesis of advanced reactive distillation technologies. This methodology allows for rapid evaluation in the initial stages of process design without relying heavily on mathematical programming-based techniques. High-level questions using first principles and heuristics underpinned a decision-making flowchart with four steps: compositions and splits; basic properties and operating windows; kinetics; phase equilibria. The flowchart provided a traffic light system to categorise the advanced reactive distillation technologies in scope as advantageous, technically feasible or not applicable. The flowchart also suggested additional, complementary technologies, producing alternative initial process flowsheets. Case studies demonstrated the suitability of advanced reactive distillation technologies for relevant chemical systems and noted the limitations of the methodology.

6.2 Conclusions

This section presents the main findings, conclusions and limitations of this research.

6.2.1 Chapter 3: Critical analysis

The synthesis and conceptual design of an intensified flowsheet containing a dual R-DWC was performed using process simulation. This conceptual design study served two purposes: 1) to investigate the relationships between mixture and reaction properties and 2) to elucidate the need for a systematic methodology to carry out the initial feasibility assessment.

The conceptual design study of a dual R-DWC evaluated boiling points and tray compositions in the liquid phase in order to find opportunities for intensification and achieve performance improvement. Boiling points were used to select the operating pressure, and tray

compositions served to locate the inlet and outlet streams. Essential information such as boiling points, compositions, and kinetics provided valuable insights to create a conceptual framework discussed in Chapter 4, which formed the basis for a more comprehensive approach to other advanced reactive distillation technologies included in this study, as demonstrated by the development of the synthesis methodology in Chapter 5.

The sensitivity analyses explored the effect of the design degrees of freedom on performance – separation, conversion and selectivity. The sensitivity analyses helped identify suitable ranges of operating conditions. By reducing the design space, time spent on design or simulation could be decreased by focusing on the most feasible solutions. This hypothesis underpinned the development of a procedure for building operating windows appropriate to advanced reactive distillation technologies detailed in Chapter 4.

Realistic and challenging features, such as dilute feeds and reactive impurities, and their potential impacts on technical feasibility and economic viability were considered. The study showed that reactive impurities in the feed could form additional byproducts, leading to yield loss and increasing the complexity of downstream processing compared to designs based on oversimplified assumptions.

The design problem was addressed using a combination of techniques, including a decomposition approach, shortcut calculations, rigorous simulation, and heat integration. The performance of the novel flowsheet was assessed using sustainability metrics to enable a fair comparison to benchmark processes from the research literature. However, the lack of appropriate metrics for estimating capital costs creates an incomplete basis for comparison.

Chapter 3 made certain assumptions that were reasonable for an initial assessment of the flowsheet performance. For example, pressure drop across the columns was not considered as structured packing (MellapakPlus 252Y in lieu of Katapak-SP that is not available in Aspen Plus) was selected because of the operating pressure (mild vacuum) and the low liquid rates. The F-factors for the esterification and hydrolysis sections of the column range from 1.37 to 2.44 $\text{Pa}^{0.5}$ and 1.34 to 3.19 $\text{Pa}^{0.5}$, respectively, corresponding to negligible pressure drops. However, a significant pressure drop could cause uneven pressure distribution across the column, which can affect flow distribution and separation efficiency.

A pseudo-homogeneous kinetic model was used to describe a kinetically controlled reaction. Mass transport between the liquid and vapour phases was described with an equilibrium model. However, inaccuracies may arise in estimating the reaction rate and activation energy,

especially when neglecting the adsorption term. An inaccurate reaction model could lead to the selection of inappropriate operating conditions and incorrect equipment sizing, which can impact capital and operating costs. Therefore, care should be taken when using the apparent reaction rate constant using a power law model, or an engineer could consider using a kinetic subroutine in Fortran or Aspen Custom Modeler.

Commercial simulators do not provide models to simulate advanced reactive distillation technologies, as highlighted in the challenges for their synthesis and design in the literature review. Assuming a fully thermally-coupled configuration equivalent to an R-DWC with negligible heat transfer through the wall, the RadFrac model in Aspen Plus was used. However, this approach may lead to incompatible heights on both sides of the wall, making the design implementation infeasible. This issue could be overcome by selecting appropriate packing for each section to provide the required HETP that can physically fit in a single shell.

6.2.2 Chapter 4: Critical analysis

Chapter 4 used various inputs to develop a procedure for building operating windows to identify suitable operating regions for advanced reactive distillation technologies. These inputs include thermodynamic properties, kinetic parameters, and constraints from the conceptual framework, the learnings from the sensitivity analyses in Chapter 3, and heuristics from conventional distillation, reactive distillation, and reactive separations, as well as those identified in the literature review for advanced reactive distillation technologies.

The effect of complex multicomponent mixtures and reaction properties were effectively evaluated in an operating window by proposing a new concept: representative components. Selecting two representative components – light and heavy – helped locate boundaries within which feasible operational regions are likely to be contained.

The procedure for building operating windows applied heuristics to account for the effects of mixture and reaction properties on the advanced reactive distillation technologies. For example, efficient use of utilities and avoidance of thermal degradation, as well as an economic compression ratio in an R-HiDiC, are captured by the location of the sliding window. This new concept expands the operating window boundaries and offers insights into the selection of technologies. Overall, operating windows tailored for advanced reactive distillation technologies can aid process development and provide a foundation for more rigorous design activities.

Reliance on data gathered from the literature can lead to inaccuracies when determining the boundaries of operating windows due to a lack of understanding of the mixture and reaction properties. For instance, in the case study for the production of lactic acid, monomethyl succinate was identified as the heavy representative component, but its property data is scarce. Lactic acid, the second heaviest representative component, was used instead, considering their similar boiling points and the likelihood of monomethyl succinate appearing in small quantities. However, lesser-known components may significantly impact if present in larger quantities. Hence, caution should be exercised when making assumptions; exploring a range of scenarios could provide insight into the impact of these uncertainties on design feasibility and performance.

6.2.3 Chapter 5: Critical analysis

A novel synthesis methodology is proposed in the form of a decision-making flowchart. This methodology supports qualitative ranking of design options during process synthesis, particularly for advanced reactive distillation technologies that have not been considered in established process synthesis approaches. The methodology serves three purposes: 1) to facilitate early-stage assessment of the technical feasibility of advanced reactive distillation technologies, 2) to categorise them as advantageous, technically feasible or not applicable and 3) to inform the development of basic process flowsheets that satisfy the design objectives.

To facilitate the application of the high-level questions formulated in the conceptual framework in Chapter 4, a logical sequence was established by structuring them into four categories in the synthesis methodology that are answered using thermodynamic properties, kinetic parameters, and constraints. However, this methodology does not consider certain properties such as miscibility gaps, distillation regions, reactive azeotropes or their dependence on operating conditions and composition. Although these properties are relevant, dismissing their existence could result in infeasible solutions. It is recommended that a more in-depth examination of these characteristics be conducted once potential advantages and disadvantages have been identified through an initial screening.

The synthesis methodology accounts for features relevant to industrial applications, such as azeotropes, impurities, multicomponent mixtures, difficult separations and side reactions. These features can be evaluated by setting up different scenarios. Failing to consider such complex features could result in simplistic flowsheet alternatives that are unable to overcome

them, leading to inefficient processes. For example, the case study for TAME production showed that side reactions could significantly impact the size of the operating window and affect the selection of technologies.

Evaluating reaction rates is challenging due to factors affecting their values, such as initial concentrations, type of catalyst, solvents used, and kinetic experiments. The synthesis methodology uses the forward reaction rate constant for an initial assessment (assuming the reaction rate follows a power law model) instead of the actual reaction rate. Directly comparing reaction rates does not allow a fair comparison between different chemical systems operating at different conditions. This simplification could introduce inaccuracies as concentrations and the reaction order are not considered, leading to erroneous sizing and selection of operating conditions, especially at the design stage.

For evaluating 'kinetics', the forward rate of reaction constant is clustered as slow, intermediate, or fast, using cutoff values expressed in orders of magnitude, which may overlap, allowing a flexible comparison during the screening procedure. The forward rate of reaction constant is evaluated at 90 °C, which may seem arbitrary, and the maximum reaction temperature. However, these values were chosen as a way to compare several systems at some temperature near the operating range and avoid introducing additional variables at an early stage.

The category 'phase equilibria' in the synthesis methodology evaluates homogeneous azeotropes at atmospheric pressure. However, it is also noted when azeotropes appear or disappear within the identified range of pressures. While this approach may lead to selecting unfeasible technologies, the decision-making matrix used in the methodology enables updating the results and reassessing the ranking of technologies to derive alternative process flowsheets.

In all case studies in Chapter 5, R-DWC was found to be either advantageous or technically feasible. This outcome could be attributed to the fact that most studies involved multicomponent mixtures with multiple products, which is a characteristic that favours R-DWC. On the other hand, the other technologies in scope have more niche applications, such as very fast reactions where side reactions must be avoided (R-HiGee), relatively slow reactions that require longer residence times (CCD), chemical systems that span a short range of boiling points to avoid a costly compression task (R-HiDiC) or to overcome azeotropes that are not consumed inside the reactive distillation column (MA-RD).

When navigating the decision-making flowchart, inaccuracies based on numerical values may arise when the value lies close to the threshold. To overcome this issue, alternative scenarios could be evaluated, as exemplified by the case study for the methyl acetate system. R-DWC was found to be the most advantageous in all scenarios. However, other technologies were deemed advantageous, feasible or even not applicable depending on the conditions selected. Inaccuracies may arise when the values used for evaluation are far off the operating range, where optimal values can be evaluated in later stages of process design.

The dependency on data gathered from the literature can pose a challenge, especially when the information is not easily accessible. In the case study for hydrogenation of benzene to produce cyclohexane, kinetic data are scarce, particularly for the reaction in the liquid phase, the type of catalyst and side reactions which can pose difficulties in accurately determining the operating windows. For example, the reaction rate order for the hydrogenation of benzene is within the temperature range evaluated in the operating window, but reference values for side reactions are provided under conditions outside these ranges. Although the side reactions cannot be represented in the operating windows due to the lack of data, identifying the type of reactions could provide guidance for selecting technologies that could help prevent side reactions when evaluating the 'kinetics' category.

6.3 Recommendations for future work

Recommendations for future work are presented to address some of the limitations of this work, its scope and underlying assumptions. Long-term opportunities for potential research are also presented to contribute to the research area.

- As discussed earlier, dependency on data gathered from the literature poses a challenge for the application of the methodology as information about the chemical systems could be incomplete, not fully described, inaccessible or non-existent. Therefore, ranges of values or appropriate estimation methods, such as correlations, could be used for early-stage screening. Then, once promising alternative solutions are identified, detailed analysis and experimental work can be planned accordingly.
- Application of the synthesis methodology proposed in this thesis to complex chemical systems that feature multicomponent feeds of varying compositions or complex reaction networks is not possible. Evaluating whether such complex systems might beneficially apply advanced reactive distillation technologies would require a thorough understanding of the phenomena involved. This limitation can be addressed in future

work by evaluating whether lumped properties for pseudo-components or a set of reactions expressed in an overall reaction can represent the behaviour of the chemical system without excluding components at an early stage. Nevertheless, deriving useful lumped properties or an overall representative reaction may still require a complete set of validated thermodynamic and kinetic data to avoid oversimplification that is not applicable to such complex systems.

- The factors affecting reaction rates (e.g., mass transfer limitations) make their evaluation difficult in a general approach such as the one presented in this thesis. In the case of heterogeneously catalysed systems, it is known that the effect of the adsorption step in the reaction can be significant, which is not often captured by the apparent rate of reaction. This limitation can be addressed in future work, taking this methodology to incorporate a “mass transfer limitations” evaluation that considers mass transfer resistances, especially those occurring in the solid catalyst.
- A deeper understanding of multi-scale phenomena and interactions is needed for simultaneous reaction and distillation in the presence of additional intensification features of the technologies studied in this thesis. Future research can focus on the development of reliable models to describe the behaviour of advanced reactive distillation technologies, enabling performance evaluation.
- The proposed approach could be extended to include other intensified reactive distillation technologies, such as microwave-assisted reactive distillation, ultrasound-assisted reactive distillation, or reactive enzymatic distillation, which offer significant promise given the development of hardware at laboratory scale and modelling investigations (Kiss et al., 2019). A deeper understanding of the governing phenomena and driving forces of these technologies can lead to defining additional high-level questions that result in decision points that can help identify their suitability.
- The synthesis methodology provides a qualitative ranking of the technical feasibility of advanced reactive distillation technologies. Further research on the process design stage requires suitable quantitative metrics for operating and capital costs and sustainability to obtain complete and tested designs to evaluate the performance of advanced reactive distillation technologies critically against conventional operations and provide further information to sustain the selection of technologies.
- The methodology developed in this thesis focused on the process synthesis stage. Future research could focus on the development of approaches for dynamic behaviour

evaluation and control strategies of highly integrated units, such as advanced reactive distillation technologies. In this manner, a deeper understanding of the operation would further enable preparation for potential commercial implementation.

6.4 References

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