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

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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 temperature limits to favour the main reaction over 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.

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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 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

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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 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. (2014) 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 S1, *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 was 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, Damköhler 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., 2022). Findings of operating windows include identification of suitable ranges for operating conditions and insights to appraise ARDT during process synthesis. Results from the application of this study contribute to 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, case studies for methyl acetate production, lactic acid purification and tert-amyl methyl ether production demonstrate the application of the operating windows.

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). Fig. 1 highlights the additional governing PI domains for five ARDT,

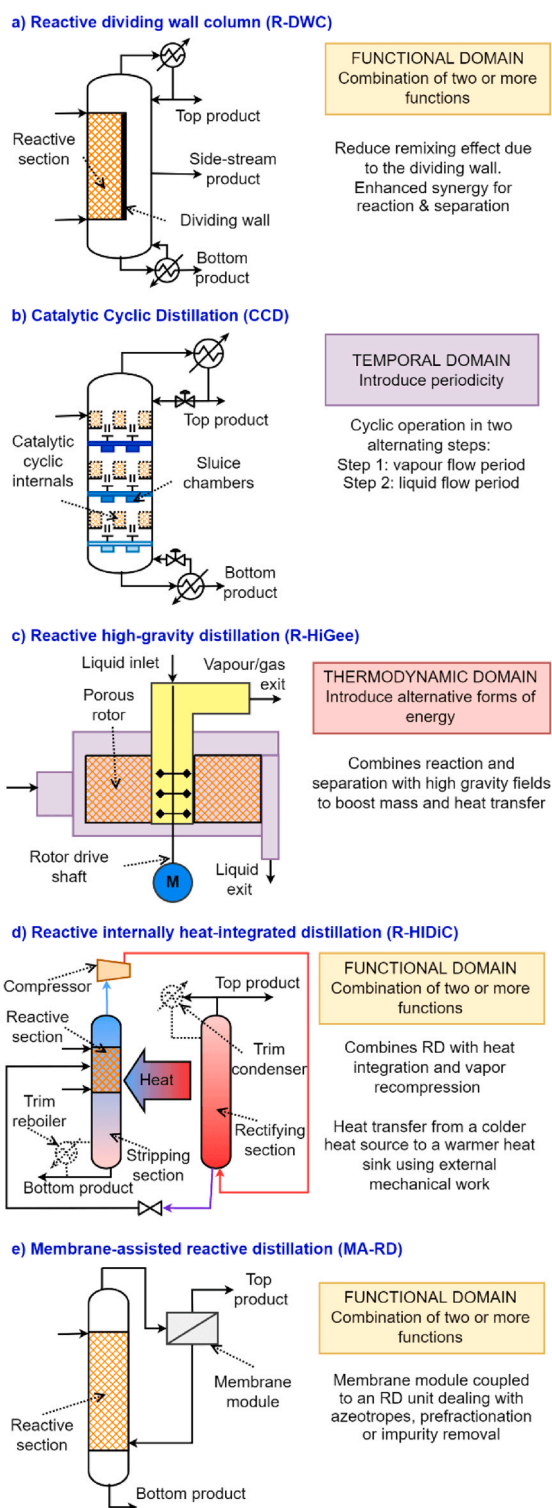


Fig. 1 – Advanced reactive distillation technologies and their governing process intensification domains.

Adapted from [Quarderer et al. \(2000\)](#); [Lutze and Gorak \(2013\)](#); [Kiss et al. \(2019\)](#).

along with a brief description. 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.

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 discussed.

3.1. New features for advanced reactive distillation assessment using operating windows

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 multi-component 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.

3.1.1.1. 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.

3.1.1.2. 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.

3.1.1.3. 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.

3.1.1.4. Selecting the light and heavy representative components. The decision-making flowchart in Fig. 2 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 understanding 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.

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 S2 in the

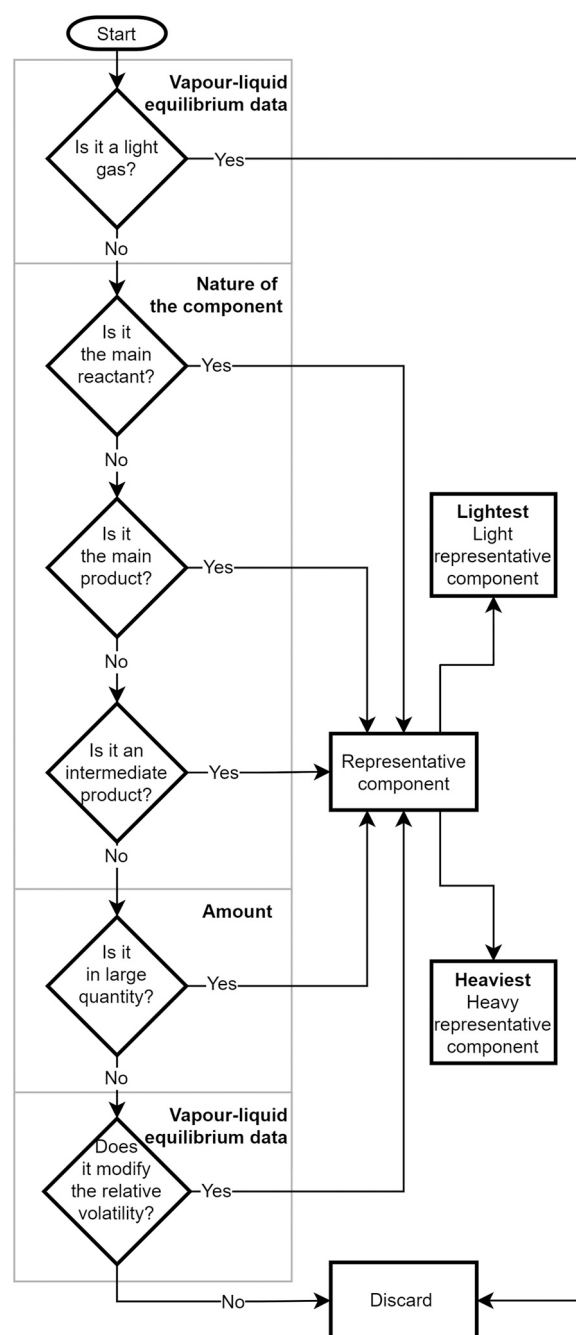


Fig. 2 – Flowchart to identify the representative components.

Supplementary Information. The intersection of the sides with the vapour pressure curve of the light (or heavy) representative components allows detecting suitable operating points. The ΔT_b is important because it is a characteristic of the chemical system and could be used while searching for suitable operating regions for reaction and separation.

3.2. Operating windows to evaluate advanced reactive distillation technologies

3.2.1. Input data required to construct the operating windows
3.2.1.1. 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.

3.2.1.2. Kinetic parameters for the main and side reactions. According to the Arrhenius 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.

3.2.1.3. 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; Patrut et al., 2014). 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.

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 S3 in the *Supplementary Information*, and the main features of the operating window are illustrated in Fig. 3. 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 methods 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 20–30 °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 120–150 °C, medium-pressure steam (10 bar) at 180 °C and high-pressure steam (40–50 bar) at 250–265 °C (Smith, 2016). The flowchart and explanation in Figure S4 in the *Supplementary Information* provide further information.

Finally, the operating window is presented as a shaded region in Fig. 3, 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:

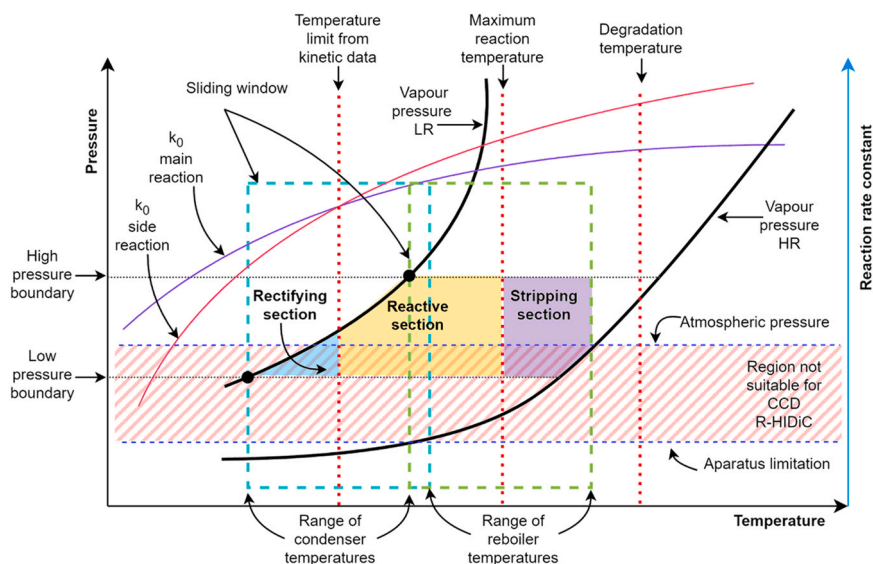


Fig. 3 – Main features of the operating windows.

- 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 S5 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.

3.3. Scope and limitations of the operating windows

The operating windows are used 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 (non-reactive) mass separating agent typically used in fluid separations – that promotes an equilibrium-limited reaction that facilitates the separation.

Considerations that are not captured when constructing the operating windows include the inability to fully explore the 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 is not guaranteed, hence the need for further evaluation of the overall process performance.

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

Table 1 – 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).

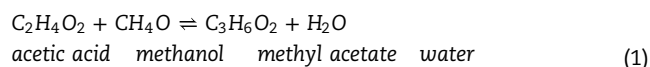
^b Li et al. (2017).

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.

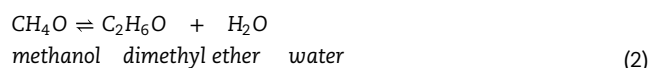
4.1. Case study 1: methyl acetate production

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 (1) and the dehydration of methanol into dimethyl ether (DME) (2). Table S1 in the Supplementary Information presents the kinetic parameters for both reactions. 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).



(1)



(2)

4.1.2. Operating windows applied to methyl acetate production

Table 1 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 Fig. 4, 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

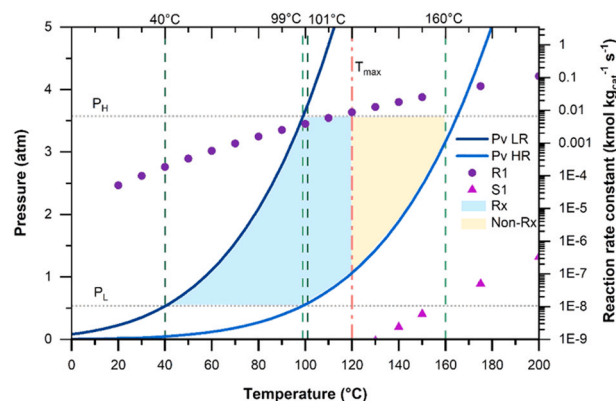


Fig. 4 – Operating windows for the methyl acetate system (Pv LR: vapour pressure of the light representative component, Pv HR: vapour pressure of the heavy representative component, R1: reaction rate constant for main reaction, S1: reaction rate constant for side reaction, Rx: reactive zone, Non-Rx: non-reactive zone, P_H: high-pressure boundary, P_L: low-pressure boundary, T_{max}: maximum reaction temperature).

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 Fig. 4) 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.

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 Fig. 4, where the reactive and non-reactive sections are shaded. The operating bounds for the methyl acetate system are summarised in Table 2.

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

Table 3 – 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).

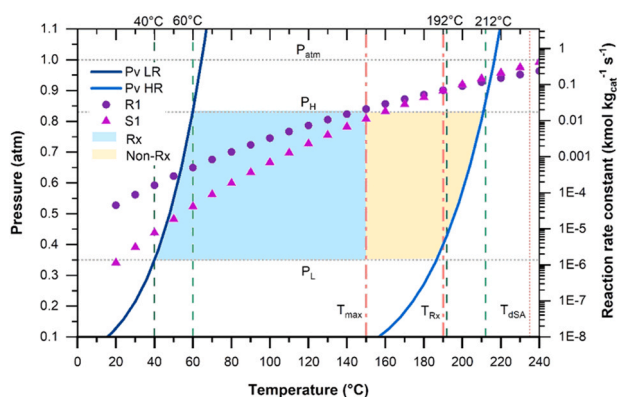


Fig. 5 – Operating window for the lactic acid system (P_{atm} : atmospheric pressure, T_{Rx} : temperature limit for reactions, T_{dSA} : degradation temperature of succinic acid).

Table 4 – 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

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 Fig. 5. The operating bounds obtained from the operating window are summarised in Table 4. 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.

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 Fig. 3, 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 temperature is possible in case catalysts with better thermal resistance are available. Regarding limitations due to 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 oligomerisation 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

Table 5 – Scenario 1 for TAME production: basic property data and nature of the components.

Components	Nature	NBP (°C)	Critical temperature (°C)	Critical pressure (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

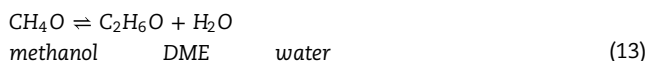
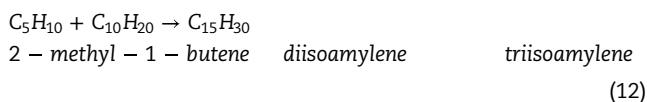
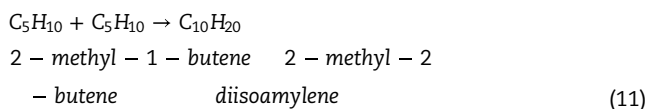
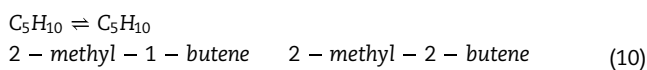
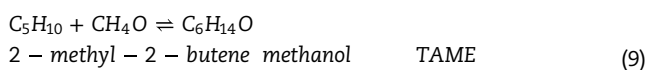
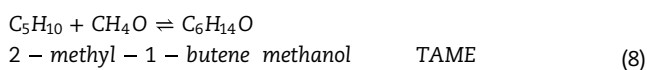
^a Morton et al. (2011)

those of poorly characterised species to allow analysis in the event that reliable data is not available.

4.3. Case study 3: tert-amyl methyl ether production

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 (8) and 2M2B (9) and one isomerisation reaction between 2M1B and 2M2B (10) (Luyben and Yu, 2008). Possible side reactions include the formation of dimers (11) and trimers (12) of 2M1B and 2M2B (Cruz et al., 2007) and methanol condensation to dimethyl ether (13) (Subawalla and Fair, 1999). The reactions are catalysed by a solid catalyst (Amberlyst 35). Table S3 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 Klöker 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.

4.3.2. Scenario 1: TAME production disregarding side reactions

Table 5 presents the basic properties and the nature of the components, listed in increasing normal boiling point order. Reactants and the product TAME 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 rectification 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 (Fig. 6, a). The temperature bounds for the reboiler temperature are 18 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.

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) (Fig. 6, 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

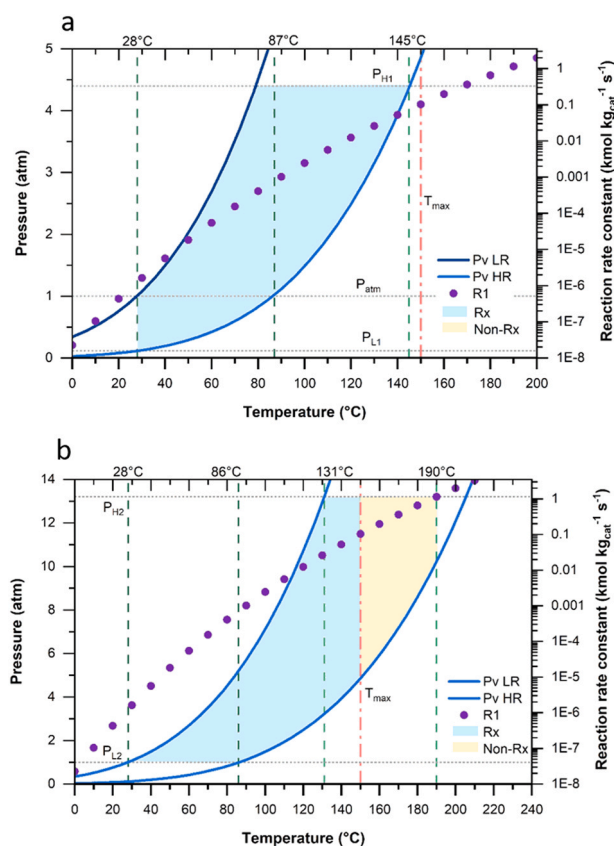


Fig. 6 – TAME case (Scenario 1): operating windows for the low-pressure stripping section (a) and high-pressure rectifying section (b) (P_{H1} : high-pressure boundary for the stripping section, P_{L1} : low-pressure boundary for the stripping section, P_{H1} : high-pressure boundary for the rectifying section, P_{L1} : low-pressure boundary for the rectifying section).

indicates that higher temperatures favour the reaction. Thus, the reactive section is more likely to be in the high-pressure rectifying section.

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 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 S3 in the Supplementary Information Table 6 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 triisooamylene production are the largest among the main and side reactions; these are represented using the secondary vertical axis in Fig. 7. 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.

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 7.

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 Fig. 7(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,

Table 6 – 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)

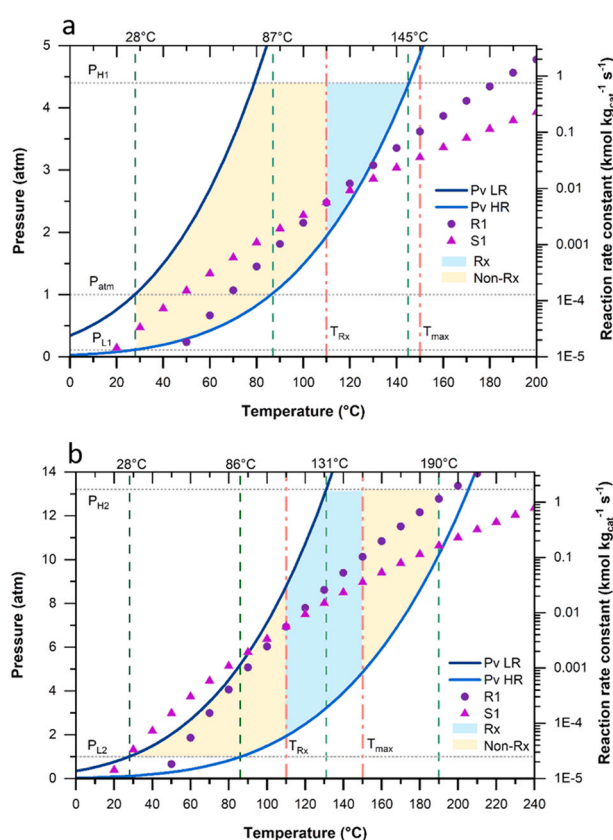


Fig. 7 – TAME case (Scenario 2): operating windows for single unit operation or rectification section (a) and stripping section (b).

Table 7 – 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

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.

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 ARDT include the evaluation of new chemical systems and suitable metrics to critically evaluate the performance.

The development of processes that involve new chemical and biochemical routes or catalysts can make the collection of physico-chemical data difficult and expensive. Thus, the lack of data would make it difficult to apply the proposed methodology for new chemical systems or processes that are under investigation. At the same time, this offers opportunities for the development of new internals or 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.

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 multi-component 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 multi-component 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 by products. 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 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.

Declaration of Competing Interest

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

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.cherd.2022.11.048](https://doi.org/10.1016/j.cherd.2022.11.048).

References

- Al-Arfaj, M.A., Luyben, W.L., 2002. Comparative control study of ideal and methyl acetate reactive distillation. *Chem. Eng. Sci.* 57, 5039–5050. [https://doi.org/10.1016/S0009-2509\(02\)00415-3](https://doi.org/10.1016/S0009-2509(02)00415-3)
- Alves de Oliveira, R., Komesu, A., Vaz Rossell, C.E., Maciel Filho, R., 2018. Challenges and opportunities in lactic acid bioprocess design—from economic to production aspects. *Biochem. Eng. J.* 133, 219–239. <https://doi.org/10.1016/j.bej.2018.03.003>
- An, D., Cai, W., Xia, M., Zhang, X., Wang, F., 2015. Design and control of reactive dividing-wall column for the production of methyl acetate. *Chem. Eng. Process. Intensif.* 92, 45–60. <https://doi.org/10.1016/j.cep.2015.03.026>
- Azapagic, A., Millington, A., Collett, A., 2006. A methodology for integrating sustainability considerations into process design. *Chem. Eng. Res. Des.* 84, 439–452. <https://doi.org/10.1205/cherd05007>
- Babi, D.K., Lutze, P., Woodley, J.M., Gani, R., 2014. A process synthesis-intensification framework for the development of sustainable membrane-based operations. *Chem. Eng. Process. Intensif.* 86, 173–195. <https://doi.org/10.1016/j.cep.2014.07.001>
- Berre, C.L., Serp, P., Kalck, P., Torrence, G.P., 2014. Acetic Acid. In: Ullmann's Encyclopedia of Industrial Chemistry, pp. 1–34. https://doi.org/10.1002/14356007.a01_045.pub3
- Campbell, J.C., Wigal, K.R., Van Brunt, V., Kline, R.S., 2008. Comparison of energy usage for the vacuum separation of acetic acid/acetic anhydride using an internally heat integrated distillation column (HIDiC). *Sep. Sci. Technol.* 43, 2269–2297. <https://doi.org/10.1080/01496390802151617>
- Cruz, V.J., Bringué, R., Cunill, F., Izquierdo, J.F., Tejero, J., Iborra, M., Fité, C., 2006. Conversion, selectivity and kinetics of the liquid-phase dimerisation of isoamylenes in the presence of C1 to C5 alcohols catalysed by a macroporous ion-exchange resin. *J. Catal.* 238, 330–341. <https://doi.org/10.1016/j.jcat.2005.12.019>
- Cruz, V.J., Izquierdo, J.F., Cunill, F., Tejero, J., Iborra, M., Fité, C., Bringué, R., 2007. Kinetic modelling of the liquid-phase dimerization of isoamylenes on Amberlyst 35. *React. Funct. Polym.* 67, 210–224. <https://doi.org/10.1016/j.reactfunctpolym.2006.11.003>
- European Commission, 2006. European Union Risk Assessment Report: 2-methoxy-2-methylbutane (TAME). European Commission – Joint Research Centre, Italy.
- Gao, X., Wang, F., Li, H., Li, X., 2014. Heat-integrated reactive distillation process for TAME synthesis. *Sep. Purif. Technol.* 132, 468–478. <https://doi.org/10.1016/j.seppur.2014.06.003>
- Harmsen, J., Verkerk, M., 2020. *Process Intensification: Breakthrough in Design, Industrial Innovation Practices, and Education*. De Gruyter.
- Hessel, V., Kralisch, D., Kockmann, N., 2014. *Novel Process Windows: Innovative Gates to Intensified and Sustainable Chemical Processes*. Wiley.
- Holtbruegge, J., Kuhlmann, H., Lutze, P., 2014. Conceptual design of flowsheet options based on thermodynamic insights for (reaction-) separation processes applying process intensification. *Ind. Eng. Chem. Res.* 53, 13412–13429. <https://doi.org/10.1021/ie502171q>

- Joglekar, H.G., Rahman, I., Babu, S., Kulkarni, B.D., Joshi, A., 2006. Comparative assessment of downstream processing options for lactic acid. *Sep. Purif. Technol.* 52, 1–17. <https://doi.org/10.1016/j.seppur.2006.03.015>
- Khunnonkwao, P., Boontawan, P., Haltrich, D., Maischberger, T., Boontawan, A., 2012. Purification of l-(+)-lactic acid from pretreated fermentation broth using vapor permeation-assisted esterification. *Process Biochem.* 47, 1948–1956. <https://doi.org/10.1016/j.procbio.2012.07.011>
- Kim, S.Y., Kim, D.M., Lee, B., 2017. Process simulation for the recovery of lactic acid using thermally coupled distillation columns to mitigate the remixing effect. *Korean J. Chem. Eng.* 34, 1310–1318. <https://doi.org/10.1007/s11814-017-0009-1>
- Kiss, A.A., 2019. Novel catalytic reactive distillation processes for a sustainable chemical industry. *Top. Catal.* 62, 1132–1148. <https://doi.org/10.1007/s11244-018-1052-9>
- Kiss, A.A., 2017. 4. Process intensification by reactive distillation. In: *Process Synthesis and Process Intensification Methodological Approaches*. De Gruyter, Berlin, Boston. <https://doi.org/10.1515/9783110465068-004>
- Kiss, A.A., 2013. *Advanced Distillation Technologies: Design Control, and Applications*. Wiley, Chichester, West Sussex, United Kingdom.
- Kiss, A.A., Jobson, M., Gao, X., 2019. Reactive distillation: stepping up to the next level of process intensification. *Ind. Eng. Chem. Res.* 58, 5909–5918. <https://doi.org/10.1021/acs.iecr.8b05450>
- Kiss, A.A., Olujić, Ž., 2014. A review on process intensification in internally heat-integrated distillation columns. *Chem. Eng. Process. Process. Intensif.* 86, 125–144. <https://doi.org/10.1016/j.cep.2014.10.017>
- Kiviranta-Pääkkönen, P.K., Struckmann, L.K., Linnekoski, J.A., Krause, A.O.I., 1998. Dehydration of the alcohol in the etherification of isoamylenes with methanol and ethanol. *Ind. Eng. Chem. Res.* 37, 18–24. <https://doi.org/10.1021/ie970454d>
- Klöcker, M., Kenig, E., Górak, A., Fraczek, K., Salacki, W., Orlikowski, W., 2003. Experimental and theoretical studies of the TAME synthesis by reactive distillation. In: *Kraslawski, A., Turunen, I. (Eds.), Computer Aided Chemical Engineering, European Symposium on Computer Aided Process Engineering-13*. Elsevier, pp. 713–718. [https://doi.org/10.1016/S1570-7946\(03\)80200-6](https://doi.org/10.1016/S1570-7946(03)80200-6)
- Kraume, M., Enders, S., Drews, A., Schomäcker, R., Engell, S., Sundmacher, K., 2022. *Integrated Chemical Processes in Liquid Multiphase Systems: From Chemical Reaction To Process Design and Operation*. Walter de Gruyter GmbH & Co KG.
- Leng, R.B., Emonds, M.V.M., Hamilton, C.T., Ringer, J.W., 2012. Holistic route selection. *Org. Process Res. Dev.* 16, 415–424. <https://doi.org/10.1021/op200264t>
- Li, H., Meng, Y., Li, X., Gao, X., 2016. A fixed point methodology for the design of reactive distillation columns. *Chem. Eng. Res. Des.* 111, 479–491. <https://doi.org/10.1016/j.cherd.2016.05.015>
- Li, Y., Zhou, S., Li, J., Ma, Y., Chen, K., Wu, Y., Zhang, Y., 2017. Experimental study of the decomposition of acetic acid under conditions relevant to deep reservoirs. *Appl. Geochem.* 84, 306–313. <https://doi.org/10.1016/j.apgeochem.2017.07.013>
- Lutze, P., Gorak, A., 2013. Reactive and membrane-assisted distillation: recent developments and perspective. *Chem. Eng. Res. Des.* 91, 1978–1997. <https://doi.org/10.1016/j.cherd.2013.07.011>
- Luyben, W.L., 2013. *Distillation Design and Control Using Aspen Simulation*, 2nd ed. Wiley, Hoboken, N.J.
- Luyben, W.L., Yu, C.-C., 2008. *Reactive Distillation Design and Control*. Wiley-Blackwell, Hoboken, N.J.
- Maleta, B.V., Shevchenko, A., Bedryk, O., Kiss, A.A., 2015. Pilot-scale studies of process intensification by cyclic distillation. *AIChE J.* 61, 2581–2591. <https://doi.org/10.1002/aic.14827>
- Marcilly, C., 2005. *Acido-basic Catalysis: Application to Refining and Petrochemistry*. Editions Technip.
- Miller, C., Fosmer, A., Rush, B., McMullin, T., Beacom, D., Suominen, P., 2017. Industrial production of lactic acid. In: *Reference Module in Life Sciences*. Elsevier. <https://doi.org/10.1016/B978-0-12-809633-8.09142-1>
- Morton, T.H., Weber, K.H., Zhang, J., 2011. Thermal decomposition of t-amyl methyl ether (TAME) studied by flash pyrolysis/supersonic expansion/vacuum ultraviolet photoionization time-of-flight mass spectrometry. *Int. J. Mass Spectrom.* 306, 210–218. <https://doi.org/10.1016/j.ijms.2010.11.003>
- Moulijn, J.A., Stankiewicz, A., 2017. Process Intensification. In: *Abraham, M.A. (Ed.), Encyclopedia of Sustainable Technologies*. Elsevier, Oxford, pp. 509–518. <https://doi.org/10.1016/B978-0-12-409548-9.10242-8>
- Orjuela, A., Santaella, M.A., Molano, P.A., 2016. Process intensification by reactive distillation. In: *Segovia-Hernández, J.G., Bonilla-Petriciolet, A. (Eds.), Process Intensification in Chemical Engineering: Design, Optimization and Control*. Springer International Publishing, Cham, pp. 131–181. https://doi.org/10.1007/978-3-319-28392-0_6
- Pasetti, M., Invernizzi, C.M., Iora, P., 2014. Thermal stability of working fluids for organic Rankine cycles: an improved survey method and experimental results for cyclopentane, isopentane and n-butane. *Appl. Therm. Eng.* 73, 764–774. <https://doi.org/10.1016/j.applthermaleng.2014.08.017>
- Pazmiño-Mayorga, I., Jobson, M., Kiss, A.A., 2021. Conceptual design of a dual reactive dividing wall column for downstream processing of lactic acid. *Chem. Eng. Process. - Process. Intensif.* 164, 108402. <https://doi.org/10.1016/j.cep.2021.108402>
- 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.), Computer Aided Chemical Engineering, 14 International Symposium on Process Systems Engineering*. Elsevier, pp. 643–648. <https://doi.org/10.1016/B978-0-323-85159-6.50107-X>
- Pérez Cisneros, E.S., Gani, R., Michelsen, M.L., 1997. Reactive separation systems—I. Computation of physical and chemical equilibrium. *Chem. Eng. Sci.* 52, 527–543. [https://doi.org/10.1016/S0009-2509\(96\)00424-1](https://doi.org/10.1016/S0009-2509(96)00424-1)
- Pöpken, T., Steingeweg, S., Gmehling, J., 2001. Synthesis and hydrolysis of methyl acetate by reactive distillation using structured catalytic packings: Experiments and simulation. *Ind. Eng. Chem. Res.* 40, 1566–1574. <https://doi.org/10.1021/ie0007419>
- Porterfield, J.P., Bross, D.H., Ruscic, B., Thorpe, J.H., Nguyen, T.L., Baraban, J.H., Stanton, J.F., Daily, J.W., Ellison, G.B., 2017. Thermal decomposition of potential ester biofuels. Part I: Methyl acetate and methyl butanoate. *J. Phys. Chem. A* 121, 4658–4677. <https://doi.org/10.1021/acs.jpca.7b02639>
- Pulido, J.L., Martínez, E.L., Maciel, M.R.W., Filho, R.M., 2011. Heat integrated reactive distillation column (r-HIDiC): Implementing a new technology distillation. *Chem. Eng. Trans.* 24, 1303–1308. <https://doi.org/10.3303/CET1124218>
- Quarderer, G.J., Trent, D.L., Stewart, E.J., Tirtowidjojo, D., Mehta, A.J., Tirtowidjojo, C.A., 2000. Method for synthesis of hypo-halous acid. *US6048513A*.
- Recker, S., Skiborowski, M., Redepenning, C., Marquardt, W., 2015. A unifying framework for optimization-based design of integrated reaction-separation processes. *Comput. Chem. Eng.* 81, 260–271. <https://doi.org/10.1016/j.compchemeng.2015.03.014>
- Riese, J., Grünwald, M., 2020. Challenges and opportunities to enhance flexibility in design and operation of chemical processes. *Chem. - Ing. - Tech.* 92, 1887–1897. <https://doi.org/10.1002/cite.202000057>
- Schembecker, G., Tlatlik, S., 2003. Process synthesis for reactive separations. *Chem. Eng. Process. Process. Intensif.* 42, 179–189. [https://doi.org/10.1016/S0255-2701\(02\)00087-9](https://doi.org/10.1016/S0255-2701(02)00087-9)
- Smith, J., Hong-Shum, L., 2003. *Food Additives Data Book*. John Wiley & Sons.
- Smith, R., 2016. *Chemical process design and integration*, 2nd ed. Wiley-Blackwell, Chichester, West Sussex, United Kingdom.
- Stankiewicz, A., Gerven, T.V., Stefanidis, G., 2019. *The fundamentals of process intensification*. Wiley VCH.
- Starr, J.N., Westhoff, G., 2014. Lactic Acid. In: *Ullmann's Encyclopedia of Industrial Chemistry*. John Wiley & Sons, Ltd, pp. 1–8. https://doi.org/10.1002/14356007.a15_097.pub3

- Steimel, J., Harrmann, M., Schembecker, G., Engell, S., 2014. A framework for the modeling and optimization of process superstructures under uncertainty. *Chem. Eng. Sci.* 115, 225–237. <https://doi.org/10.1016/j.ces.2013.04.052>
- Steimel, J., Harrmann, M., Schembecker, G., Engell, S., 2013. Model-based conceptual design and optimization tool support for the early stage development of chemical processes under uncertainty. *Comput. Chem. Eng.* 59, 63–73. <https://doi.org/10.1016/j.compchemeng.2013.06.017>
- Su, C.-Y., Yu, C.-C., Chien, I.-L., Ward, J.D., 2013. Plant-wide economic comparison of lactic acid recovery processes by reactive distillation with different alcohols. *Ind. Eng. Chem. Res.* 52, 11070–11083. <https://doi.org/10.1021/ie303192x>
- Subawalla, H., Fair, J.R., 1999. Design guidelines for solid-catalyzed reactive distillation systems. *Ind. Eng. Chem. Res.* 38, 3696–3709. <https://doi.org/10.1021/ie990008l>
- Sundmacher, K., Kienle, A., 2003. *Reactive Distillation: Status and Future Directions*. Wiley VCH, Weinheim.
- Suphanit, B., 2010. Design of internally heat-integrated distillation column (HIDiC): Uniform heat transfer area versus uniform heat distribution. *Energy* 35, 1505–1514. <https://doi.org/10.1016/j.energy.2009.12.008>
- Turton, R., 2018. *Analysis, synthesis, and design of chemical processes*, 5th ed. Prentice Hall, Boston.
- Tylko, M., Barkmann, S., Sand, G., Schembecker, G., Engell, S., 2006. Synthesis of reactive separation processes. In: Schmidt-Traub, H., Górak, A. (Eds.), *Integrated Reaction and Separation Operations: Modelling and Experimental Validation*. Springer, Berlin, Heidelberg, pp. 7–94. https://doi.org/10.1007/3-540-30304-9_2
- Vanaki, A., Eslamloueyan, R., 2012. Steady-state simulation of a reactive internally heat integrated distillation column (R-HIDiC) for synthesis of tertiary-amyl methyl ether (TAME). *Chem. Eng. Process. Process. Intensif.* 52, 21–27. <https://doi.org/10.1016/j.cep.2011.12.005>
- Wacker, 2022. Methyl acetate [WWW Document]. Wacker. URL <https://www.wacker.com/h/en-gb/solvents/methyl-acetate-metac-97/p/000000209> (accessed 8.11.22).
- Werth, K., Lutze, P., Kiss, A.A., Stankiewicz, A.I., Stefanidis, G.D., Górak, A., 2015. A systematic investigation of microwave-assisted reactive distillation: Influence of microwaves on separation and reaction. *Chem. Eng. Process. Process. Intensif.* 93, 87–97. <https://doi.org/10.1016/j.cep.2015.05.002>
- Zuo, C., Pan, L., Cao, S., Li, C., Zhang, S., 2014. Catalysts, kinetics, and reactive distillation for methyl acetate synthesis. *Ind. Eng. Chem. Res.* 53, 10540–10548. <https://doi.org/10.1021/ie500371c>
- Patrut, C., Bildea, C.S., Lita, I., Kiss, A.A., 2014. Cyclic distillation - Design, control and applications, *Separation & Purification Technology*. 125, 326–336. <https://doi.org/10.1016/j.seppur.2014.02.006>