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# A systematic framework for assessing the applicability of reactive distillation for quaternary mixtures using a mapping method

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## Keywords

Feasibility assessment, conceptual design, process synthesis, azeotropic systems

## Highlights

- New systematic framework for evaluating the applicability of reactive distillation
- Mapping method is used to screen reactive distillation designs in non-ideal systems
- Case studies covering non-ideal quaternary systems with various boiling point ranking

## Abstract

Reactive distillation (RD) is a useful process intensification technique used in the chemical process industries as it offers important advantages such as energy and cost savings, relative to conventional technologies. However, industrial application of RD is still limited by the complexity of designing and understanding such a complex process. While simple, robust shortcut design methods that require only basic information (such as the relative volatility of components) exist for conventional distillation, such methods for evaluating the applicability of RD are not yet established.

This work fills this gap by presenting a new systematic framework for assessing the RD applicability based on a mapping method. The method enables RD designs to be screened using only relative volatilities and chemical equilibrium constant as input data. The evaluation focuses on reactions involving four components ( $A + B \rightleftharpoons C + D$ ) with various boiling point orders, which are of most industrial importance. The proposed systematic framework is validated through its application to five case studies, (trans-)esterifications presenting various separation challenges due to the formation of azeotropes. This novel approach offers a valuable aid for engineers in taking an educated go/no-go decision in the very initial stages of conceptual design, before performing any rigorous simulations of RD flowsheets.

1

## 2 **1. Introduction**

3 Process intensification – comprising the development of apparatus and techniques in the  
4 chemical industries – is crucial for delivering cheaper, smaller, more energy-efficient, safer  
5 and sustainable technologies (Stankiewicz and Moulijn, 2000). It also paves the way to fulfill  
6 the chemical industry demands, especially in the context of globalization and sustainability  
7 (Charpentier, 2007). Among the available process intensification units, reactive distillation  
8 (RD), which integrates reaction and separation in a single column, as illustrated in Figure 1,  
9 has demonstrated significant contribution to process efficiency (Kiss et al., 2019).

10 The benefits of reactive distillation, compared to conventional technologies involving a  
11 sequence of reaction and separation units, include: 1) increased conversion and selectivity, 2)  
12 lower capital investment due to the reduced number of the process units, 3) significant energy  
13 savings, by utilizing the heat of exothermic reactions for vaporization, and 4) reduced health,  
14 safety and environmental risks because of lower emissions, avoidance of reactor hot spots and  
15 reduces risk of runaway reactions (Tuchlenski et al., 2001; Harmsen, 2007; Shah et al., 2012;  
16 Kiss, 2016, 2017).

17 Over the past decade, over 1,000 research manuscripts explored the development of reactive  
18 distillation (Wierschem and Górak, 2018; Kiss, 2019), considering modelling of RD for  
19 specific systems (Khan and Adewuyi, 2019), process optimization and control (Sneesby et al.,  
20 1997; Sharma and Singh, 2010), pilot-scale experiments (Keller et al., 2012), the selection of  
21 catalysts and operating parameters for desired reactions (Chiu et al., 2006; Kiss et al., 2008)  
22 and column internals (Subawalla et al., 1997; Götze et al., 2001).

23 Nevertheless, commercial application of reactive distillation remains challenging due to the  
24 complexities in the synthesis, design, and operation of RD columns (Chen et al., 2000; Li et  
25 al., 2012; Li et al., 2016). Multiple interactions between vapor-liquid equilibrium, mass  
26 transfer, intra-catalyst diffusion in heterogeneous catalyzed processes and chemical kinetics  
27 inhibit the rapid assessment of reactive distillation designs (Taylor and Krishna, 2000).

28 Various methods for designing RD systems have emerged since the late 1980s; these can be  
29 classified as graphical, optimization and heuristic approaches (Barbosa and Doherty, 1988a;  
30 Barbosa and Doherty, 1988b; Almeida-Rivera et al., 2004; Kiss, 2016, 2017). For example,  
31 Lee et al. (2000) developed a graphical approach, based on the modified Ponchon-Savarit and  
32 McCabe-Thiele methods, to assess the location of reactive zones in reactive distillation for  
33 binary reactions. Urselmann et al. (2011) introduced a memetic algorithm to optimize the  
34 design of reactive distillation for the production of methyl tert-butyl ether, concerning the

1 total annual cost. Subawalla and Fair (1999) suggested guidelines, based on a generic  
2 standpoint and heuristic approaches, for determining the design parameters of reactive  
3 distillation in solid-catalyzed systems. Other design methods are reported in the open  
4 literature (including Ung and Doherty, 1995; Giessler et al., 1998; They et al., 2005;  
5 Damartzis and Seferlis, 2010; Jantharasuk et al., 2011; Amte et al., 2013; Kiss, 2016, 2017).  
6 However, the results of rigorous calculations and simulations in those methods are usually  
7 only applied to a certain reaction system; repetitive calculations are required to evaluate  
8 reactive distillation for other chemical systems. Therefore, designing a reactive distillation  
9 process can be time-consuming and complex (Segovia-Hernández et al., 2015).

10 In conventional distillation processes, shortcut models are used to initialize column designs.  
11 Models, such as the Fenske-Underwood-Gilliland method, determine the minimum number of  
12 theoretical stages, minimum reflux ratio and number of theoretical stages required for a given  
13 reflux ratio. The models employ relative volatility of compounds ( $\alpha$ ) to characterize the  
14 separation performance in the column. The relative volatility can be quantified from the feed  
15 composition. Alternatively, it can be taken as an average value at the top and bottom streams  
16 based on their compositions. Non-ideal vapour-liquid equilibrium behavior in the system  
17 reduces the accuracy of the shortcut models' predictions; greater errors are generally observed  
18 in more non-ideal systems (Smith, 2016). However, the shortcut models are robust and can be  
19 solved quickly (Towler and Sinnott, 2012), and hence, are a good basis for generating initial  
20 column designs and for initializing rigorous models. To the best of our knowledge, unlike for  
21 conventional distillation, methods that use some key parameters to evaluate reactive  
22 distillation designs are not well established. Rigorous simulations and calculations are usually  
23 needed to investigate the applicability of reactive distillation to each reaction system.

24 The present work proposes a new systematic framework for assessing the applicability of  
25 reactive distillation to azeotropic (non-ideal) quaternary reaction systems,  $A + B \rightleftharpoons C + D$ ,  
26 with various rankings of boiling points, only based on hypothetical and ideal cases using few  
27 key parameters, namely relative volatilities of compounds, chemical equilibrium constants  
28 and Damköhler number. The approach is called the mapping method, and it was introduced  
29 by our prior study (Muthia et al., 2018a), but the scope of that study was limited to ideal  
30 quaternary reaction systems for only a subset of boiling point orders,  $T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$ .  
31 The mapping method features a plot of reflux ratio vs. number of theoretical stages to define  
32 an 'applicable region', in which reactive distillation could potentially be employed for a  
33 certain chemical system. The applicability of reactive distillation is assessed using pre-  
34 prepared applicability graphs of 'generic' cases, corresponding to hypothetical components

1 and ideal reaction systems. To assess a ‘real’ system, the user needs basic information, i.e.,  
2 characteristic values of relative volatilities and the chemical equilibrium constant of the real  
3 system of interest.

4 Previous studies, such as Barbosa and Doherty (1988a, 1988b) have developed a set of  
5 transformed composition variables to calculate the minimum reflux ratios for single- and  
6 double-feeds reactive distillation columns. Giessler et al. (1998) proposed a method called  
7 statics analysis that enables the calculation of the number of theoretical stages based on  
8 thermodynamic-topological analysis of distillation diagrams. However, those methods only  
9 provide reflux ratio and the number of theoretical stages for a single configuration. This novel  
10 work provides a systematic approach to generate applicability graphs of reactive distillation  
11 (for any system of interest), which contain all possible RD configurations with various  
12 number of theoretical stages and reflux ratios. Note that only one applicability graph is  
13 generated for each chemical system and that graph can be used multiple times by end-users  
14 (engineers) to design different RD configurations.

15 The present work demonstrates the new framework by applying it to five case studies  
16 exhibiting different separation challenges arising due to the presence of azeotropes. These  
17 case studies serve to validate the proposed framework, in terms of its ability to estimate the  
18 applicable region for RD in a given quaternary system with non-ideal behaviour.

19

## 20 **2. Mapping method overview**

21 This work presents a systematic framework that applies our novel mapping method, for  
22 screening and initialization of reactive distillation column designs. The mapping method  
23 (Muthia et al., 2018a, 2019a) has been introduced and demonstrated in near-ideal quaternary  
24 systems with the reaction  $A + B \rightleftharpoons C + D$ . Initially the approach was demonstrated for systems  
25 with boiling point order  $T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$  (Muthia et al., 2018a), where the two  
26 products are the lightest (C) and heaviest (D) components in the system and so are readily  
27 separated from each other. A subsequent study demonstrated the approach for systems with  
28 other boiling point orders (Muthia et al., 2019b) and provided some insights into the optimal  
29 feed locations of reactive distillation columns.

30 The main feature of the mapping method is the applicability graph of reactive distillation  
31 designs, which is a plot of reflux ratio vs. the number of theoretical stages, as illustrated in  
32 Figure 2(a). A boundary line in an applicability graph identifies the lowest reflux ratios  
33 possible for various numbers of theoretical stages. The ‘applicable area’ represents multiple  
34 column configurations each with a certain number of rectifying, reactive and stripping stages,

1 where some very dissimilar configurations may have very similar reflux ratios for an identical  
2 number of theoretical stages. For example, see Figure S1 and Table S1 in the Supporting  
3 Information.

4 As demonstrated for near-ideal quaternary systems (Muthia et al., 2018a), the method is  
5 capable of predicting the applicability area for reactive distillation of real systems based only  
6 on pre-prepared applicability graphs of generic cases. In these idealized, hypothetical generic  
7 cases, the relative volatilities and chemical equilibrium constants are fixed and independent of  
8 process temperatures. This work aims to demonstrate that real (non-ideal) systems can also be  
9 addressed by the method, in particular for cases involving the presence of azeotropes, as these  
10 systems are industrially important.

11 Figure 2(b) illustrates application of the method: the user must select the most relevant  
12 generic cases, i.e. where the representative relative volatilities and chemical equilibrium  
13 constant are similar to those of the real system being assessed. The shaded area in Figure 2(b)  
14 represents the location in which the actual boundary line is expected to lie. Thus, the user can  
15 read from the plot approximate values of the reflux ratio and numbers of stages required in the  
16 reactive distillation column. Note that the mapping method predicts the number of theoretical  
17 stages and reflux ratio, but not the column configuration. The multiple possible  
18 configurations represent an opportunity for reactive distillation column design.

19 Figure 3 summarizes the methodology developed in this work, which has three directions for:  
20 (1) the generation of applicability maps, (2) the validation of the maps using case studies, and  
21 (3) the actual use of the generic maps by end-users to determine the applicability of reactive  
22 distillation for new cases. For the purpose of the validation of the proposed method, in this  
23 study, the generation of generic applicability graphs is only performed for relevant generic  
24 cases with the representative relative volatilities and chemical equilibrium constants that are  
25 similar to those of case studies.

26 The generation of generic applicability graphs and the validation of the mapping method in  
27 this study require extensive simulations for both generic cases and case studies, in which  
28 reactive distillation configurations are generated in Aspen Plus process simulation software  
29 using the RadFrac model. In the simulations for the generation of generic maps, hypothetical  
30 chemical components A, B, C and D are defined, the ideal property model is selected, and the  
31 boiling points and the Antoine coefficients of defined hypothetical components are changed  
32 for the specified relative volatilities set. Next, fixed equilibrium (and reaction rate) constants  
33 are input to the simulation software. An equimolar feed of the reactants (A and B) is fed to a  
34 reactive distillation column in which each separation stage is assumed to reach phase

1 equilibrium and each reactive stage is assumed to reach both reaction and phase equilibria.  
2 The purity of the product streams is specified (99 mol%), i.e. the overall material balance is  
3 fixed. The mixture is modelled as an ideal mixture but the column is modelled rigorously –  
4 material and energy balances are carried out on each stage, informed by equilibrium  
5 calculations.  
6 Note that the simulations are all carried out for a ‘simple’ reactive distillation, with a structure  
7 such as that shown in Figure 1(a). The column operates at atmospheric pressure with fixed  
8 feed inlets at the top and the bottom stages of the reactive section. To obtain multiple  
9 configurations, the numbers of rectifying, reactive and stripping stages are varied for each  
10 number of theoretical stages by using the sensitivity analysis block. For each configuration,  
11 the optimization tool in Aspen Plus is simultaneously employed to minimize the reflux ratio  
12 under the constraint of product purity  $\geq 99$  mol%. Among all possible configurations, the  
13 lowest reflux ratio is manually selected for each number of theoretical stages. The lowest  
14 energy for all numbers of theoretical stages form a boundary line of an applicability area.  
15 To validate the method, in this study, the predictions of the applicability graph are compared  
16 with the results of rigorous simulations for the case studies. These simulations, carried out in  
17 Aspen Plus, take into account real chemical components, the phase equilibrium behavior (i.e.  
18 constant relative volatility is not assumed) and reaction behavior (e.g. reaction kinetics or  
19 dependence of equilibrium conversion with temperature and composition are accounted for).  
20 Similar to that conducted for the generic case, sensitivity and optimization blocks, are  
21 employed for the case study, in which various column configurations – with various numbers  
22 of rectifying, stripping and reactive stages – are modelled for different numbers of theoretical  
23 stages. Once again, the feed is assumed to be an equimolar mixture of the reactants (A and B)  
24 and the purity of the products is fixed at 99 mol%. Depending on the properties of the  
25 mixture, various configurations may be explored. For example, feed stages at other locations  
26 than the top and bottom of the reactive zone may be selected and a liquid-liquid phase  
27 separator may be included, as shown in Figure 1(b), if it is anticipated that the overhead  
28 product is a low-boiling heterogeneous azeotrope. These validation simulations aim to  
29 identify the minimum reflux ratio required to achieve the desired material balance for a given  
30 total number of stages. The result is then compared to the boundary of the applicability region  
31 for a generic system with similar characteristic parameters (relative volatilities and reaction  
32 equilibrium constant). If the required reflux ratio for a given number of stages is similar (e.g.  
33 within 50%) for the two cases, then it is argued that the applicability map is valid – i.e. that it  
34 is sufficiently useful for process screening to allow informed go/no-go decision-making.

1 Prior to the use of the mapping method by end-users, a team of researchers or engineers, who  
2 act as map generators, produce a bundle of many generic applicability maps with different  
3 sets of fixed relative volatilities, chemical equilibrium constants and reaction rates. Once  
4 those graphs have been created through multiple simulations in Aspen Plus, further rigorous  
5 simulations are not needed to allow the graph to be used for process screening. Note that an  
6 applicability graph of a generic case prepared once by map generators can be used afterwards  
7 multiple times by process engineers to assess the applicability of reactive distillation and  
8 design different column configurations.

9 End-users employ the mapping method in a similar way to a global positioning system (GPS),  
10 where determined representative relative volatilities of compounds and calculated equilibrium  
11 constant (and the Damköhler number for a kinetically controlled reaction) are overlaid onto  
12 generic applicability graphs that are pre-generated by map generators. The graphs may then  
13 be used to quantify the reflux ratio – number of stages relationship for a real system, without  
14 requiring any detailed simulation of the real system or associated reactive distillation column.  
15 In principle, the fixed parameters of the generic system should be similar to those of the real  
16 system, to get the most useful predictions.

### 17 18 **3. Results and discussion**

19 This section focuses on formulating and testing the systematic framework, by outlining the  
20 new systematic framework developed for assessing the applicability of reactive distillation  
21 columns and exploring the effectiveness of the framework for five case studies.

#### 22 23 **3.1. A systematic framework for assessing the applicability of reactive distillation**

24 Figure 4 summarizes the workflow of the framework, showing the sequence of steps followed  
25 to obtain multiple reactive distillation configurations and to conduct a preliminary economic  
26 evaluation of a proposed reactive distillation application. The users of the systematic  
27 framework are expected to be process engineers in the chemical industries involved in the  
28 very early stages of conceptual process design, and who wish to explore the potential benefits  
29 of reactive distillation, while minimizing the engineering time required to assess options and  
30 identify potentially attractive design solutions. That is, the framework aims to help engineers  
31 support decision-making, while avoiding time-consuming rigorous process simulations.

32 The framework is designed to consider equimolar quaternary reactions ( $A + B \rightleftharpoons C + D$ ) –  
33 industrial applications have already shown reactive distillation to be an attractive technology  
34 for systems of this nature (Sharma and Mahajani, 2003; Hiwale et al., 2004). At the beginning



1 of the applicability assessment, it is crucial to identify the boiling points of the four species  
2 and to classify the quaternary mixture according to their ranking, using an established  
3 convention (Luyben and Yu, 2008). Prior studies have shown a significant impact of boiling  
4 point order on the performance of reactive distillation (Chen and Yu, 2008; Luyben and Yu,  
5 2008). In those studies, they conducted rigorous simulations and performed detailed economic  
6 calculation concerning only a fixed chemical equilibrium constant.

7 Our previous work considered a range of chemical equilibrium constants and employed a  
8 simpler approach, based on the mapping method, taking the number of theoretical stages and  
9 reflux ratio as important performance indicators for the capital investment and the energy  
10 requirement (Muthia et al., 2019b). These studies found that, in general, the likelihood of a  
11 quaternary system ( $A + B \rightleftharpoons C + D$ ) being well suited to RD increases in the following order:

- 12 • Group I<sub>r</sub>            ( $T_{b,A} < T_{b,C} < T_{b,D} < T_{b,B}$ )
- 13 • Group III<sub>r</sub>        ( $T_{b,A} < T_{b,C} < T_{b,B} < T_{b,D}$ )
- 14 • Group III<sub>p</sub>        ( $T_{b,C} < T_{b,A} < T_{b,D} < T_{b,B}$ )
- 15 • Group I<sub>p</sub>         ( $T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$ ).

16  
17 In the most suitable class of mixtures (I<sub>p</sub>), the boiling point order facilitates separation of the  
18 products C and D because they have the most extreme boiling points in the mixture.

19 Note that reactive distillation technology is not possible for equimolar reactions in groups II<sub>p</sub>  
20 ( $T_{b,C} < T_{b,D} < T_{b,A} < T_{b,B}$ ) and II<sub>r</sub> ( $T_{b,A} < T_{b,B} < T_{b,C} < T_{b,D}$ ), as, in these cases, the reactants (A  
21 and B) are both lighter than or both heavier than the products (C and D). As shown in Figure  
22 4, the first step of the framework, therefore, is to identify the extent to which reactive  
23 distillation is applicable to the mixture of interest by considering the class of mixture. For  
24 mixtures in classes I and III, the user proceeds to the next step of the flowchart.

25 Next, the user determines characteristic values of the relative volatilities, assuming the  
26 purities of products C and D are 99 mol% (where the main impurity of product C is the lighter  
27 reactant, A, and the main impurity in product D is the heavier reactant, B) and an equimolar  
28 feed (50 mol% A and B). That is, volatilities of the products and feed  $\alpha_{CA}$ ,  $\alpha_{AB}$  and  $\alpha_{BD}$  need  
29 to be calculated in group I<sub>p</sub>, for mixtures containing 99% C/1% A, 50% A/50% B and 1%  
30 B/99% D (Muthia et al., 2018a, 2019a).

31 Table 1 summarizes which volatilities need to be calculated for each class of mixture. In all  
32 cases, the volatility between reactants A and B is determined at saturated liquid conditions of  
33 the feed (with composition 50 mol% A, 50 mol% B) and the volatility between each product

1 and the closest-boiling reactant is determined at saturated liquid condition of the product (with  
2 composition 99% product, 1% reactant). Note that the method (described so far) does not  
3 account for the formation of azeotropes.

4 This paper significantly expands the scope of the mapping method to include non-ideal  
5 quaternary systems, with various boiling point orders. The presence of an azeotrope between  
6 two compounds with the closest boiling points is significant, as it may correspond to a change  
7 of volatility order, i.e. the characteristic relative volatility may be less than 1. In order to  
8 represent the difficulty (or impossibility) of separating the azeotrope-forming mixture, this  
9 work sets the relative volatility to 1.

10 As in conventional distillation, representative relative volatilities in the shortcut models may  
11 not accurately account for the significant nonideality of the systems. Based on this  
12 knowledge, this work assumes that the mapping method is unsuitable for quaternary mixtures  
13 forming more than one azeotrope between any two components influencing the value of any  
14 representative relative volatility. Specifying multiple representative relative volatilities at 1,  
15 due to the presence of azeotropes, might result in over-/underestimation of the applicability of  
16 reactive distillation. Therefore, Figure 4 shows that the flowchart rejects systems of this type  
17 as unsuitable.

18 The next step is to characterize the chemical equilibrium constant of the system. As chemical  
19 equilibrium is typically temperature dependant, a characteristic temperature needs to be  
20 selected; the method is then applied assuming that the equilibrium constant applies throughout  
21 the column. This work suggests that the equilibrium constant is calculated at the average  
22 boiling points of reactants. The logic for this is that the mixture in the reactive zone of the  
23 column will predominantly comprise the reactants, i.e. the boiling point of the mixture will lie  
24 between the boiling points of the two pure-component reactants.

25 A reaction will only achieve a low conversion if its chemical equilibrium constant is small. A  
26 low conversion in a reactive distillation column could cause reactants to accumulate in the  
27 column, thus promoting the reverse reaction(s) as well as inhibiting separation and/or  
28 requiring large reflux ratios to purify the products satisfactorily. Therefore, this work applies  
29 the heuristic that reactive distillation is not likely to be an attractive technology for systems  
30 with a very low reaction equilibrium constant, i.e.  $K_{eq} < 0.01$  (Shah et al., 2012). In these  
31 cases, conventional reaction processes or other types of hybrid processes may be more  
32 suitable. On the other hand, systems with a very high chemical equilibrium constant ( $K_{eq} >$   
33 10) strongly favour high conversion in the reactor, and therefore simultaneous separation in a  
34 distillation column may not bring a significant advantage (Shah et al., 2012). In these cases,

1 conventional reaction–separation–recycle flowsheets are likely to perform satisfactorily.  
2 Therefore, the next step of the framework suggests the range of chemical equilibrium  
3 constants that is practically relevant for reactive distillation processes, as shown in Figure 4.  
4 In spite of that recommendation, evaluating the feasibility of reactive distillation might still be  
5 useful for the system with a high chemical equilibrium constant, if a slow kinetically  
6 controlled reaction most likely occurs.

7 In real processes, the assumption of reaction equilibrium may be highly unrealistic. For  
8 example, parameters that control the reaction and separation performance of a reactive  
9 distillation column, relate to reaction kinetics and residence time. The dimensionless  
10 Damköhler (Da) number relates key parameters – the reaction rate constant ( $k_f$ ), liquid  
11 residence time ( $\tau$ ) and catalyst loading ( $\beta$ ):

12

$$Da = k_f \cdot \beta \cdot \tau \quad (1)$$

13

14 For the calculation of the Damköhler number this method takes into account the liquid  
15 residence time per stage, which is actually the ratio of the liquid hold-up per stage to the flow  
16 rate per stage. The maximum liquid residence time per stage considered is 120 seconds to  
17 enable realistic column designs, i.e. the liquid and catalyst occupy maximum 50% of the stage  
18 hold-up volume. The catalyst loading per stage ( $\beta$ ) is the volumetric ratio of the amount of  
19 catalyst to the liquid hold-up per stage. A large Da number implies fast kinetics, a long liquid  
20 residence time, a high liquid hold-up and/or a high catalyst loading, which could benefit the  
21 performance of a reactive distillation process.

22 A higher Da number increases the size of the applicability region for a given reaction, until  
23 the applicability region is effectively identical to that when it is assumed that reaction  
24 equilibrium is achieved. Overestimation of the liquid residence time, liquid hold-up or  
25 catalyst loading, however, may result in an ineffective column operation or even an unfeasible  
26 process. Determining appropriate values of those parameters is essential for realistic design of  
27 the process. Therefore, the next step in the flowchart uses the ratio of the Da number to the  
28 equilibrium constant when applying the generical applicability graphs.

29 At  $Da/K_{eq} \geq 5$ , Muthia et al. (2018a) observed that for a defined generic case with various  
30 chemical equilibrium constant values ( $K_{eqs} = 0.1, 1, 10$ ) the reactive distillation configuration  
31 of a kinetically controlled reaction is similar to that of its equilibrium-limited case, in terms of  
32 reflux ratio and the number of separation and reactive stages. Additionally, Figure S2 in the

1 Supporting Information shows that the applicability areas of both equilibrium-limited and  
2 kinetically controlled reactions are identical for two cases representing real reaction systems –  
3 synthesis of methyl acetate and hydrolysis of methyl lactate. This proves that  $Da/K_{eq}$  ratios  
4 exceeding 5 can be used practically as an initial criterion for initializing the design parameters  
5 of reactive distillation column.

6 The applicability assessment is conducted using pre-prepared graphs of a relevant generic  
7 case, i.e. with the same boiling point order and relevant values of the volatilities and  
8 equilibrium constant. Further assessment is required to obtain a preliminary economic  
9 evaluation of alternative designs. Cost estimation for reactive distillation columns can be  
10 obtained by adapting the economic evaluation procedures for conventional distillation, which  
11 are explained by Douglas (1988), Seider et al. (2010), Towler and Sinnott (2012). The  
12 Supporting Information presents some important equations used to calculating the total annual  
13 cost for conventional column.

14 Our previous work (Muthia et al., 2018b) presents the cost estimation of a reactive distillation  
15 process for amyl acetate production, using two assumptions affecting the economic aspect of  
16 the column design: 1) the cost of reactive trays is 20% higher than the cost of separation trays  
17 because of its non-standard features, and 2) the height of reactive stages is 20 to 30% larger  
18 than that of separation trays to avoid flooding or entrainment because of the presence of  
19 catalyst. The study found that the most cost-effective reactive distillation configurations lie  
20 close to the boundary line of the applicability graph of the assessed reaction system (i.e., the  
21 configurations with the lowest reflux ratios). Furthermore, it suggested that the cost of  
22 reactive distillation is more sensitive to the change of reflux ratio than the increase of number  
23 of reactive stages; a slight increase of reflux ratio could significantly affect both capital  
24 investment and energy requirement.

25 As described above, the framework presented in Figure 4 provides a systematic approach for  
26 screening a quaternary system for its suitability for reactive distillation, for estimating key  
27 design parameters, including number of stages, reflux ratio and hold-up on reactive stages,  
28 and for preliminary cost estimation of the reactive distillation column. The method is based  
29 on some very strongly simplifying assumptions. In our previous work, elements of the method  
30 were developed and demonstrated. The next section aims to explore the extent to which the  
31 method is useful for screening quaternary mixtures with non-ideal phase equilibrium  
32 behaviour.

33

### 1 **3.2. Case studies: validation of the design framework**

2 This section presents five case studies for the validation of the proposed framework presented  
3 in Figure 4, where these case studies involve non-ideal phase equilibrium behavior, i.e. the  
4 formation of homogeneous and heterogeneous azeotropes. The case studies also aim to  
5 demonstrate the advantages offered by the method, along with its limitation. The validation  
6 steps consist of: (1) preparing the applicability graph of the generic case corresponding to the  
7 key parameters of the case study (characteristic relative volatilities and chemical equilibrium  
8 constant), and (2) performing rigorous simulations for the case to evaluate the performance  
9 predicted by the methodology with that predicted using rigorous simulation.

10 The case studies belong to groups  $I_p$  ( $T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$ ),  $III_p$  ( $T_{b,C} < T_{b,A} < T_{b,D} < T_{b,B}$ )  
11 and  $III_r$  ( $T_{b,A} < T_{b,C} < T_{b,B} < T_{b,D}$ ), which offer the promising reactive distillation applications.  
12 While reactive distillation might be applicable to group  $I_r$  ( $T_{b,A} < T_{b,C} < T_{b,D} < T_{b,B}$ ),  
13 additional equipment for purifying the products is typically needed (Luyben and Yu, 2008;  
14 Muthia et al., 2018c). Therefore, reaction systems in class  $I_r$  are not explored in this work. The  
15 case studies are limited to equilibrium-limited reactions. As shown previously (Muthia et al.,  
16 2018a), the results for kinetically-controlled reactions are expected to be similar to those for  
17 equilibrium-limited reactions.

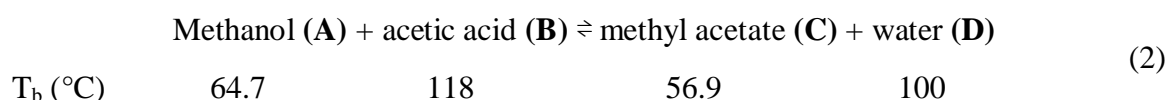
18 The suitability of the mapping method to assess quaternary systems is mainly assessed by  
19 comparing the predictions from the pre-prepared applicability graphs for generic cases and the  
20 rigorous simulation results of corresponding column configurations for real systems. The  
21 deviation between the predicted and the actual reflux ratios and numbers of theoretical stages  
22 is calculated, to provide a quantitative comparison. Note that: 1) the purpose of the  
23 framework is to accelerate the initial assessment of the suitability of reactive distillation for a  
24 given reactive system; 2) the purpose of the economic evaluation is to provide a very  
25 approximate estimate of costs to assist with decision-making about whether to continue to  
26 explore the design option in more detail. Based on our experience of working in and with  
27 industrial practitioners, we argue that there is a need for a method that provides qualitative  
28 guidance, not necessarily quantitative agreement, to evaluating the RD applicability at an  
29 early conceptual design stage in order to support a go/no-go decision.

30

#### 31 **3.2.1. Case 1: Methyl acetate synthesis by esterification**

32 Methyl acetate is widely used as a solvent for producing resins and oils. The production of  
33 methyl acetate via esterification is a prime example of successful application of reactive  
34 distillation in the chemical industries. Many researchers have used this reaction as a case

1 study for developing models and design approaches (e.g. Bessling et al., 1998; Kreul et al.,  
 2 1998; Song et al., 1998; Al-Arfaj and Luyben, 2002; Huss et al., 2003; Bangga et al., 2019).  
 3 This system is selected as a case study for validating our method because it is industrially  
 4 important and key data are available in the literature. Methyl acetate (C) and water (D) are  
 5 produced by esterification of methanol (A) and acetic acid (B), as shown in Eq. (2):



7  
 8 The mixture is in class III<sub>p</sub>. The UNIQUAC-Hayden-O'Connell property model represents the  
 9 nonideality of this system (Pöpken et al., 2000). Methyl acetate–methanol and methyl acetate–  
 10 water form homogeneous binary azeotropes; Table 2 presents their compositions and boiling  
 11 points. Table S2 in the Supporting Information provides the liquid and equilibrium vapour-  
 12 phase compositions of the feed and products . The representative relative volatilities for 99  
 13 mol% pure products are  $\alpha_{CA} = 0.52$  and  $\alpha_{DB} = 1.6$  and the feed volatility,  $\alpha_{AB} = 6.3$ . Following  
 14 the systematic framework,  $\alpha_{CA}$  is then set as 1 .

15 Eq. (3) gives the chemical equilibrium expression provided by Popken et al. (2000);  $K_{eq} =$   
 16 16.3 at the average boiling points of the reactants (91.4°C).

$$\ln(K_{eq}) = -3.82 + \frac{2408.65}{T} \quad (3)$$

18  
 19 Based on the representative key parameters of the case study, applicability graphs of generic  
 20 cases were prepared for values of  $K_{eq}$  of 10 and 20, with  $\alpha_{CA} = 1.0$ ,  $\alpha_{AB} = 6.3$ ,  $\alpha_{DB} = 1.6$ , as  
 21 depicted in Figure 5(a). The shaded area represents the region in which the 'real' boundary  
 22 line is expected to lie.

23 Figure 5 shows that the simulation results are in reasonably good agreement with the  
 24 predictions of the generic applicability graph, in which the concept of using a single reactive  
 25 distillation is identified as achievable. Figure S2 in the Supporting Information presents  
 26 applicability graphs for feed stage locations. It is found that locating the feed stages within the  
 27 reactive zone improves the column performance, as indicated by the increased size of the  
 28 applicable region. Placing the feeds within the reactive zone supports immediate reaction,  
 29 therefore lowering the chance of forming an azeotrope between methyl acetate (product C)

1 and methanol (reactant A). The solid line in Figure 5(a) shows the real boundary line for Case  
2 1, where both feed stages are within the reactive zone.

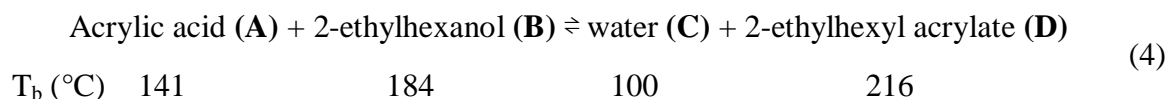
3 In spite of the formation of azeotropes, and the assumption in the applicability graph of  
4 constant relative volatility, the graph indicates that reactive distillation is applicable. In this  
5 system, classified as group III<sub>p</sub> ( $T_{b,C} < T_{b,A} < T_{b,D} < T_{b,B}$ ), product C – the lightest compound  
6 – is readily removed as the top product. The high chemical equilibrium constant enables  
7 reactant B – the heaviest compound – to be almost completely consumed before it reaches the  
8 stripping section. For example, the composition profile of a column configuration with  
9  $NTS=2 \cdot NTS_{min}$  (2 rectifying, 51 reactive and 7 stripping stages) and reflux ratio of 1.8 is  
10 given in Figure S3 in the Supporting Information.

11

### 12 **3.2.2. Case 2: 2-Ethylhexyl acrylate production via esterification**

13 2-Ethylhexyl acrylate (2-EHA) is used in the chemical process industries as a precursor of  
14 various homopolymers and copolymers. They are frequently used for the production of  
15 coatings, printing inks and adhesives (Komoń et al., 2013). The esterification reaction at the  
16 core of the 2-EHA production is shown in Eq. (4).

17



18

19 The UNIQUAC-Hayden-O'Connell property model describes the nonideality of the mixtures  
20 (Moraru and Bildea, 2018). The mixtures of water/2-ethylhexanol and water/2-EHA compose  
21 two heterogeneous binary azeotropes at specific temperatures and compositions, as listed in  
22 Table 3. The production of 2-EHA was selected as the second case study because it represents  
23 group I<sub>p</sub> ( $T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$ ) that has the most favored boiling point ranking of  
24 quaternary systems. The presence of two azeotropes in this system adds further complexities  
25 and challenges compared to the near-ideal quaternary systems in group I<sub>p</sub> that we have  
26 assessed previously (Muthia et al., 2018a, 2019a).

27 The representative relative volatilities for this case study are  $\alpha_{CA}=1.6$ ,  $\alpha_{AB}=4$  and  $\alpha_{BD}=5.3$  –  
28 see Table S3 in the Supporting Information for more details. Eq. (5) provides the correlation  
29 between the temperature change and chemical equilibrium constant; the representative  
30 chemical equilibrium constant is 19.7, at the average boiling points of reactants (162.5°C).

31

$$\ln(K_{eq}) = 8.58 - \frac{2438.50}{T} \quad (5)$$

1  
2 Figure 6(a) presents the applicability graphs of the generic cases for values of  $K_{eq}$  of 15 and  
3 25, with  $\alpha_{CA}=1.6$ ,  $\alpha_{AB}=4$  and  $\alpha_{DB}=5.3$ . Those applicability graphs are relevant to the  
4 applicability of a single RD column. The shaded area depicts the expected region where the  
5 boundary line for the case study should exist. Rigorous simulation for the case study,  
6 however, shows that there is no applicability area for the operation of a single column. The  
7 presence of a heterogeneous azeotrope between 2-ethylhexanol (reactant B) and water  
8 (product C) with a high fraction of product C ( $x_C=0.968$ ) hinders the separation of 99 mol%  
9 pure product C. Further investigation was performed resulting in the applicable heterogeneous  
10 reactive distillation configurations, as a decanter deals with the liquid-phase separation. The  
11 boundary line of the applicability graph for this setup is highlighted by the solid line in Figure  
12 6(a).

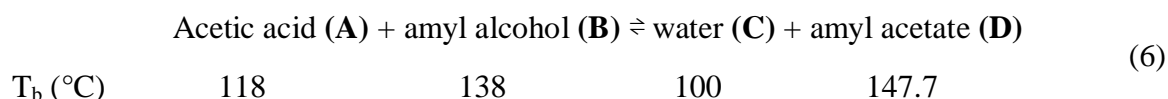
13 The assessment of this case study suggests that the mapping method is capable of predicting  
14 the applicability of RD for the systems with heterogeneous azeotrope(s) by disregarding  
15 specific types of column setup. The scope is limited in such cases, because the representative  
16 relative volatilities of the real system do not distinguish the nonideality caused by homo-  
17 and/or heterogeneous azeotropes. In most cases, RD with a decanter is needed to overcome  
18 the heterogeneous azeotrope.

19

### 20 **3.2.3. Case 3: Amyl acetate synthesis by esterification**

21 Amyl acetate is mainly used as an organic solvent, a flavoring agent and an extractant. The  
22 most common route of amyl acetate production is via esterification, as shown in Eq. (6).

23



24

25 The non-random two-liquid (NRTL) property model describes adequately the nonideality of  
26 this system (Chiang et al., 2002). The Hayden-O'Connell second virial coefficient model was  
27 used to account for the dimerization of carboxylic acids in the vapor phase. This system also  
28 belongs to group I<sub>p</sub> (just as case study 2), but it demonstrates further complexity with an  
29 increased number of azeotropes. This system contains one homogeneous binary, two



1 heterogeneous binary, one homogeneous ternary and one heterogeneous ternary azeotropes, as  
 2 presented in Table 4.

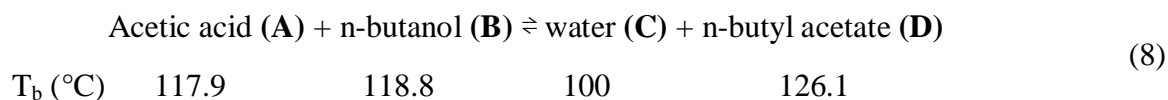
3 The representative relative volatilities for this case study are  $\alpha_{CA}=2$ ,  $\alpha_{AB}=1.7$  and  $\alpha_{BD}=1.8$  –  
 4 see Table S4 in the Supporting Information for details. Eq. (7) shows the formula of the  
 5 chemical equilibrium constant (Tang et al., 2005);  $K_{eq}=2$  at the average boiling points of both  
 6 reactants (128°C).

$$\ln(K_{eq}) = 2.63 - \frac{777.00}{T} \quad (7)$$

8  
 9 Figure 7(a) gives the applicability graphs of the generic cases for chemical equilibrium  
 10 constants of 1 and 5, with  $\alpha_{CA}=2$ ,  $\alpha_{AB}=1.7$  and  $\alpha_{BD}=1.8$ . The predicted boundary line of the  
 11 applicability area is expected to be within the shaded area and the actual boundary line of the  
 12 applicability area is indicated by the solid line. The actual and predicted applicability areas  
 13 include regions on and above their corresponding boundary lines. As observed in case study  
 14 2, due to heterogeneous azeotropes, the simulation result for this case study reveals that there  
 15 is no applicability graph for a single reactive distillation column. In this reaction, obtaining  
 16 product C with the purity  $\geq 99$  mol% is much more difficult than in the previous case study,  
 17 as the reactive distillation operation is hindered by three potential heterogeneous azeotropes  
 18 between product C and other compounds that are composed by high fractions of product C  
 19 ( $x_C > 0.82$ ). Instead, the operation of heterogeneous reactive distillation is attainable – see (a)  
 20 for the actual boundary line of this setup – because a decanter takes advantage of the liquid-  
 21 liquid split.

#### 22 23 **3.2.4. Case 4: n-Butyl acetate production via esterification**

24 Butyl acetate is used as a synthetic fruit flavoring in foods (e.g. candy, ice cream, cheese, and  
 25 baked goods) as well as a high-boiling solvent of moderate polarity. The production of n-  
 26 butyl acetate is common via the esterification route, as shown in Eq. (8).



28  
 29 The UNIQUAC property model represents well the nonideality of the system (Venimadhavan  
 30 et al., 1999), and it is associated with the Hayden-O'Connell second virial coefficient model.

1 Similar to case studies 1 and 2, this system also belongs to group I<sub>p</sub>. However, this case study  
2 possesses very non-ideal interactions between the compounds. There are six azeotropes  
3 identified in the system, including one heterogeneous ternary, two heterogeneous binary, two  
4 homogeneous binary and one homogeneous ternary azeotropes, as listed in Table 5. This case  
5 study provides more than one azeotrope between two compounds representing 99 mol% pure  
6 products and 50 mol% pure reactants. Therefore, according to the systematic framework  
7 proposed in this paper, the mapping method should not be suitable to characterize properly the  
8 relative volatilities of compounds.

9 Rigorous simulations were performed for further validation. The representative relative  
10 volatilities for this system are  $\alpha_{CA}=1.4$ ,  $\alpha_{AB}=1$  and  $\alpha_{BD}=1$  – see Table S5 in the Supporting  
11 Information for the details. The actual  $\alpha_{AB}$  for 50 mol% pure reactants and the actual  $\alpha_{CA}$  for  
12 99 mol% pure products are 0.95 and 0.57, respectively. These variables are then set as 1,  
13 following the systematic framework. Gangadwala et al. (2003) suggested the formula of the  
14 chemical equilibrium constant, as written in Eq. (9);  $K_{eq}=11.5$  at the average boiling points of  
15 both reactants (118.4°C).

16

$$\ln(K_{eq}) = 1.3404 + \frac{430.804}{T} \quad (9)$$

17

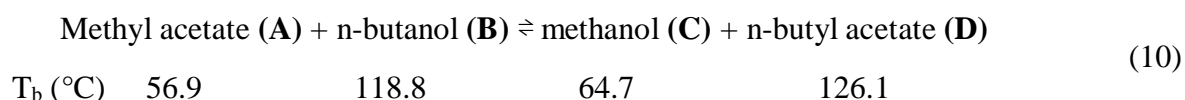
18 The simulation of the generic cases for  $K_{eq}$ s of 10, 15 and 20 with  $\alpha_{CA}=1.4$ ,  $\alpha_{AB}=1$  and  $\alpha_{BD}=1$   
19 generated no applicability graphs. The finding is acceptable considering the separation  
20 difficulty with very strict relative volatilities of compounds.

21 A set of simulation carried out for the case study confirmed that there is no applicability graph  
22 obtained for a single RD column. On the other hand, the simulation result suggested that  
23 heterogeneous RD applies to this system. The applicability graph for this setup is presented in  
24 Figure 8(a). This finding highlights a mismatch between the prediction based on the generic  
25 cases and the results obtained from the rigorous simulation of the case study. The result  
26 indicates that the method is unsuitable for the systems with more than one azeotrope between  
27 two compounds that represent 99 mol% pure products and 50 mol% pure reactants because  
28 multiple characteristic relative volatilities set as 1, concerning the presence of azeotropes,  
29 might underestimate the applicability of reactive distillation.

30

### 1 3.2.5. Case 5: Transesterification of methyl acetate and n-butanol

2 Methyl acetate is a cheap by-product in the production of polyvinyl alcohol (PVA). It can be  
 3 converted by transesterification to methanol (a feedstock of the same synthesis route to PVA)  
 4 and n-butyl acetate (which is widely used as an important extractive agent, a synthetic fruit  
 5 flavoring and a solvent in plastics, resins, and gums industries). The transesterification  
 6 reaction between methyl acetate and butanol is given in Eq. (10).



8  
 9 This reaction was selected as case study because it represents another classification of boiling  
 10 point rankings in quaternary reactions, namely group III<sub>r</sub> ( $T_{b,A} < T_{b,C} < T_{b,B} < T_{b,D}$ ). This  
 11 group may pose a critical challenge for purifying product C at the top stream, especially when  
 12 the chemical equilibrium constant is considerably low. The UNIQUAC property model  
 13 represents the nonideality of the case study (Božek-Winkler and Gmehling, 2006). There are  
 14 two homogeneous azeotropes identified between two compounds that represent 99 mol% pure  
 15 products, which are methyl acetate/methanol (reactant A / product C) and n-butanol/n-butyl  
 16 acetate (reactant B / product D), as shown in Table 6. According to the systematic framework,  
 17 the mapping method should be not suitable for the assessed case study.

18 For further validation, rigorous simulations were performed for both generic cases and the  
 19 case study. The representative relative volatilities of this case study for 99 mol% pure  
 20 products and 50 mol% pure reactants are  $\alpha_{AC}=3.4$ ,  $\alpha_{AB}=12$  and  $\alpha_{BD}=1.9$  – see Table S6 in the  
 21 Supporting Information for details. Božek-Winkler and Gmehling (2006) provide the  
 22 chemical equilibrium constant expression, as given in Eq. (11). The representative chemical  
 23 equilibrium constant is 1.08 at the average boiling points of two reactants (87.9°C).

$$\ln(K_{eq}) = 0.8158 - \frac{267.9}{T} \quad (11)$$

25  
 26 The applicability graphs of generic cases were prepared for values of  $K_{eq}$  of 1 and 2 with  
 27  $\alpha_{AC}=3.4$ ,  $\alpha_{AB}=12$  and  $\alpha_{BD}=1.9$ , and the actual boundary line for the case study is expected to  
 28 be within the shaded area in Figure 8(b). Rigorous simulation of the case study, however,  
 29 suggested that there is no applicability graph found for a single RD column or any standalone  
 30 RD setup without additional process equipment, for the targeted purity  $\geq 99$  mol%. Published

1 literature confirmed that the reactive distillation operation to achieve a high product purity for  
2 this reaction is only feasible if it is assisted with membrane technology (Steinigeweg and  
3 Gmehling, 2004). The mismatch between the expectation from pre-prepared generic graphs  
4 and the simulation results of the case study is caused by an overestimation of the  
5 representative relative volatilities of the case study.

### 7 **3.3. Analysis of the applicability prediction by the mapping method**

8 The validation carried out in the previous section highlighted the suitability of the mapping  
9 method for non-ideal quaternary systems. Three case studies showed that the method is  
10 capable of providing the first screening of reactive distillation designs for high product purity,  
11 i.e.,  $\geq 99$  mol%. Two case studies showed that the method is unsuitable for the systems with  
12 more than one azeotrope that represents 99 mol% pure products and 50 mol% pure reactants.  
13 In that instance, the use of the mapping method over-/under-estimates the RD designs.

14 An additional assessment was performed to quantify the deviations between the prediction  
15 and the actual numbers of theoretical stages based on the generic cases, for the configurations  
16 with  $NTS=2 \cdot NTS_{min}$ . The selection of these configurations was only based on our previous  
17 knowledge in the classic distillation process. Indeed, other configurations with  $RR=1.2 \cdot RR_{min}$ ,  
18 or with any other considerations, can be evaluated. Using the interpolation technique, the  
19 predicted numbers of theoretical stages and reflux ratios of the case studies, at  
20  $NTS=2 \cdot NTS_{min}$ , are given in Figure 5(b) for case 1, Figure 6(b) for case 2, Figure 7(b) for  
21 case 3. All triangle markers in these figures show the numbers of theoretical stages and all  
22 square markers provide the corresponding reflux ratios. Filled triangle and square markers  
23 give the actual values obtained from rigorous simulations of the case studies.

24 The results obtained from the interpolation were compared to the actual numbers of  
25 theoretical stages and reflux ratios of the case studies. All deviations were quantified based on  
26 the absolute differences between numbers of theoretical stages or reflux ratios over the actual  
27 value obtained from the rigorous simulation of the case study, as listed in Table 7. The  
28 deviations are reasonably acceptable for case studies 1 and 3, for the assessment at the very  
29 early stage of conceptual design level. Large deviations ( $> 50\%$ ) were obtained for case 2,  
30 because of small numbers of theoretical stages and low reflux ratios. Although percentage  
31 wise there are some differences, in terms of absolute numbers the values are very useful for an  
32 early industrial assessment of RD applicability.

1 Overall, the method gives satisfying results regarding the applicability prediction of reactive  
2 distillation. The method is useful for engineers in the chemical industries to obtain a go-/no  
3 decision prior to performing rigorous simulations of real systems.

#### 4 5 **4. Conclusions**

6 This novel systematic framework proposed here is valuable in assessing the applicability of  
7 reactive distillation for non-ideal quaternary systems, using as basis a mapping method that  
8 was introduced and developed in our prior work for near-ideal systems (Muthia et al., 2018a,  
9 2019a, 2019b). When reactive distillation is applicable, multiple column configurations and a  
10 preliminary economic evaluation are obtained for an assessed chemical system. The  
11 sequential steps in the workflow consist of the recognition of the group of boiling point  
12 rankings, the calculation of the key relative volatilities and chemical equilibrium constant of  
13 the real system to select the most relevant pre-prepared applicability graphs of generic cases  
14 and the preliminary economic evaluation. For kinetically controlled reactions, the  
15 determination of catalyst loading, liquid residence time or liquid hold-up is based on an initial  
16 criterion of  $Da / K_{eq} \geq 5$ , so that one can estimate the values of those design parameters to  
17 obtain the optimum RD design.

18 The use of the systematic framework has been successfully validated using five case studies  
19 that represent different groups of boiling point ranking in quaternary systems, and have  
20 distinctive separation complexities due to azeotropes. The boiling point rankings give a  
21 significant effect on the RD performance. As shown in case studies 1-4, having a product as  
22 the lightest compound is favored, so the product can be easily collected at the top stream with  
23 high purity. The given case studies proved that the applicability of reactive distillation is  
24 significantly affected by the nonideality of the systems which is indicated by the number and  
25 the types of azeotropes present. Reactive distillation with a decanter might be considered if  
26 heterogeneous azeotropes exist between the lightest product and the other compounds.

27 The validation of the approach using case studies 1-3 showed that the framework is suitable  
28 also for complex systems with only one azeotrope between two compounds that represent 99  
29 mol% pure products and 50 mol% pure reactants. Representative relative volatilities  
30 calculated for 99 mol% pure products and 50 mol% pure reactants correspond to the desired  
31 product compositions and the equimolar feed of reactants. The proposed approach is capable  
32 of predicting the applicability of reactive distillation by disregarding the types of column  
33 setup, for instance, if a decanter is needed to overcome heterogeneous azeotropes. By only  
34 referring to some basic parameters, the systematic framework allows engineers in the

1 chemical industries to reduce the number of rigorous simulations required in the early  
2 conceptual design stage.

3 The validation of the approach using case studies 4 and 5 showed that the framework is  
4 unsuitable for strongly non-ideal systems with multiple azeotropes present between two  
5 components affecting representative relative volatilities. The limitation of the proposed  
6 method is analogous to that of shortcut methods for conventional distillation (such as Fenske-  
7 Underwood-Gilliland), where assumed constant relative volatilities are unable to provide  
8 accurate initial column designs for the separation of strongly non-ideal systems.

9

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14

15

## 16 **Nomenclature**

17	$K_{eq}$	chemical equilibrium constant [-]
18	$NTS$	number of theoretical stages [-]
19	$NTS_{min}$	minimum number of theoretical stages [-]
20	$RR$	reflux ratio [mol/mol]
21	$RR_{min}$	minimum reflux ratio [mol/mol]
22	$T_b$	boiling point temperature [°C]
23	$x_i$	mol fraction of compound i
24	$\alpha_{ij}$	relative volatility between compounds i and j [-]
25	$\Delta H_r^\circ$	heat of reaction [kJ/mol]

26

27

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- 12

1 **Table**

2 **Table 1.** Summary of characteristic volatilities for quaternary mixtures of groups I and III

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Group	Boiling point order	Volatility order	Characteristic product volatilities
I <sub>p</sub>	$T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$	$C > A > B > D$	Distillate: $\alpha_{CA}$ (99% C, 1% A) Bottoms: $\alpha_{BD}$ (1% B, 99% D)
III <sub>p</sub>	$T_{b,C} < T_{b,A} < T_{b,D} < T_{b,B}$	$C > A > D > B$	Distillate: $\alpha_{CA}$ (99% C, 1% A) Bottoms: $\alpha_{DB}$ (99% D, 1% B)
III <sub>r</sub>	$T_{b,A} < T_{b,C} < T_{b,B} < T_{b,D}$	$A > C > B > D$	Distillate: $\alpha_{AC}$ (1% A, 99% C) Bottoms: $\alpha_{BD}$ (1% B, 99% D)
I <sub>r</sub>	$T_{b,A} < T_{b,C} < T_{b,D} < T_{b,B}$	$A > C > D > B$	Distillate: $\alpha_{AC}$ (1% A, 99% C) Bottoms: $\alpha_{DB}$ (99% D, 1% B)

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18 **Table 2.** Molar composition of the azeotropes and corresponding boiling points in the system  
19 containing methanol, acetic acid, methyl acetate and water at 1 atm

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No.	Type	Boiling point (°C)	Methanol (A)	Acetic acid (B)	Methyl acetate (C)	Water (D)
1	Homogeneous	53.7	0.341	-	0.659	-
2	Homogeneous	56.4	-	-	0.890	0.110

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**Table 3.** Molar composition of the azeotropes and corresponding in the system containing acrylic acid, 2-ethylhexanol, water and 2-ethylhexyl acrylate at 1 atm

No.	Type	Boiling point (°C)	Acrylic acid (A)	2-ethylhexanol (B)	Water (C)	2-ethylhexyl acrylate (D)
1	Heterogeneous	99.1	-	0.032	0.968	-
2	Heterogeneous	99.6	-	-	0.984	0.016

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**Table 4.** Molar composition of the azeotropes and corresponding in the system containing acetic acid, amyl alcohol, water and amyl acetate at 1 atm

No.	Type	Boiling point (°C)	Acetic acid (A)	Amyl alcohol (B)	Water (C)	Amyl acetate (D)
1	Heterogeneous	94.7	-	0.044	0.823	0.133
2	Heterogeneous	94.9	-	-	0.830	0.170
3	Heterogeneous	95.9	-	0.148	0.852	-
4	Homogeneous	139.9	0.218	0.585	-	0.197
5	Homogeneous	140.3	0.260	0.740	-	-

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**Table 5.** Molar composition of the azeotropes and corresponding in the system containing methyl acetate, n-butanol, methanol and n-butyl acetate at 1 atm

No.	Type	Boiling point (°C)	Acetic acid (A)	n-Butanol (B)	Water (C)	n-Butyl acetate (D)
1	Heterogeneous	90.1	-	0.107	0.690	0.203
2	Heterogeneous	90.9	-	-	0.715	0.285
3	Heterogeneous	92.7	-	0.243	0.757	-
4	Homogeneous	114.7	-	0.647	-	0.353
5	Homogeneous	120.8	0.537	0.150	-	0.313
6	Homogeneous	123.4	0.537	0.463	-	-

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**Table 6.** Molar composition of the azeotropes and corresponding in the system containing methyl acetate, n-butanol, methanol and n-butyl acetate at 1 atm

No.	Type	Boiling point (°C)	Methyl acetate (A)	n-Butanol (B)	Methanol (C)	n-Butyl acetate (D)
1	Homogeneous	53.7	0.659	-	0.341	-
2	Homogeneous	116.9	-	0.780	-	0.220

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1 **Table 7.** Comparison of predicted and actual numbers of theoretical stages and reflux ratios  
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No.	Case studies	Number of theoretical stages / [-]			Reflux ratio / [mol/mol]		
		Predicted	Actual	Deviation	Predicted	Actual	Deviation
1	Case 1	40	60	33%	1.94	1.63	19%
2	Case 2	15	8	88%	0.80	0.39	105%
3	Case 3	29	20	45%	1.90	1.54	23%

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1 **Figure captions** (auto-updated)

2 Figure 1. Schematic representation of (a) a single reactive distillation column and (b) a  
3 heterogeneous reactive distillation column.

4 Figure 2. (a) An illustrative applicability graph of reactive distillation and (b) an illustrative  
5 prediction of the applicability of reactive distillation to a reaction system, based on generic  
6 cases – the actual boundary line is predicted to be within the shaded area.

7 Figure 3. Methodology developed for the generation of the applicability graphs of reactive  
8 distillation, the validation of the mapping method and the use of the method by end-users.

9 Figure 4. Systematic framework for assessing the applicability of reactive distillation.

10 Figure 5. Case 1 – methyl acetate production via esterification (a) The predicted boundary line  
11 of the RD applicability within the shaded area and the actual boundary line of the RD  
12 applicability indicated by the solid line; (b) Reflux ratio and the number of theoretical stages:  
13 solid points = estimate; open points = rigorous simulation results.

14 Figure 6. Case 2 – 2-ethylhexyl acetate synthesis via esterification (a) The predicted boundary  
15 line of the RD applicability within the shaded area and the actual boundary line of the RD  
16 applicability indicated by the solid line; (b) Reflux ratio and the number of theoretical stages:  
17 solid points = estimate; open points = rigorous simulation results.

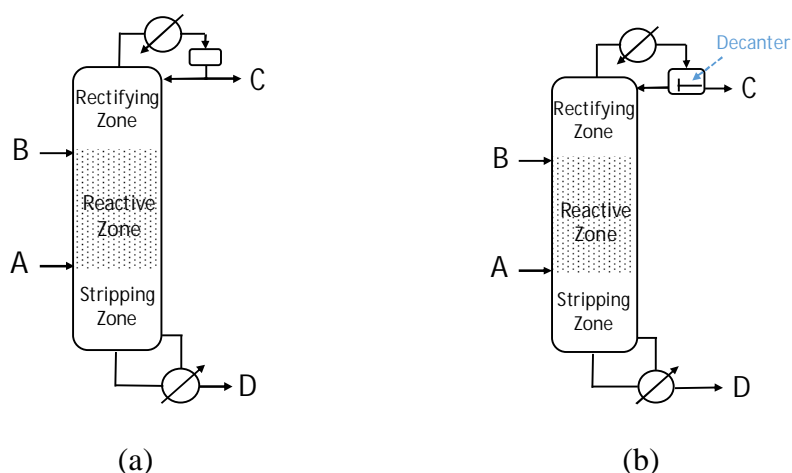
18 Figure 7. Case 3 – amyl acetate production via esterification (a) The predicted boundary line  
19 of the RD applicability within the shaded area and the actual boundary line of the RD  
20 applicability indicated by the solid line; (b) Reflux ratio and the number of theoretical stages:  
21 solid points = estimate; open points = rigorous simulation results.

22 Figure 8. (a) The actual boundary line of the applicability area of case 4 – butyl acetate  
23 synthesis via esterification – for a heterogeneous reactive distillation setup and (b) the  
24 predicted boundary line of the applicability area of case 5 – transesterification of methyl  
25 acetate and butanol – within the shaded area.

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4 **Figure 1.** Schematic representation of (a) a single reactive distillation column and (b) a  
5 heterogeneous reactive distillation column.

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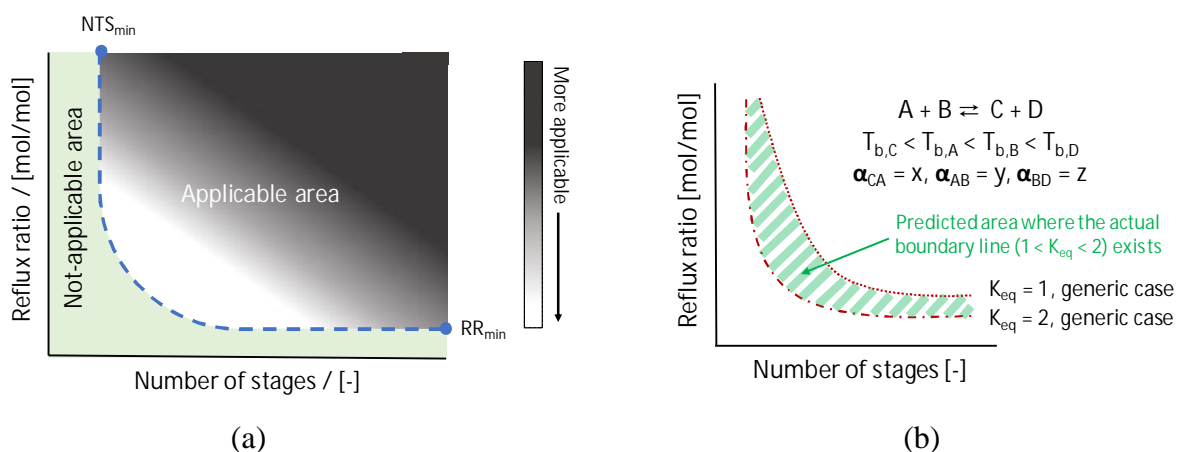
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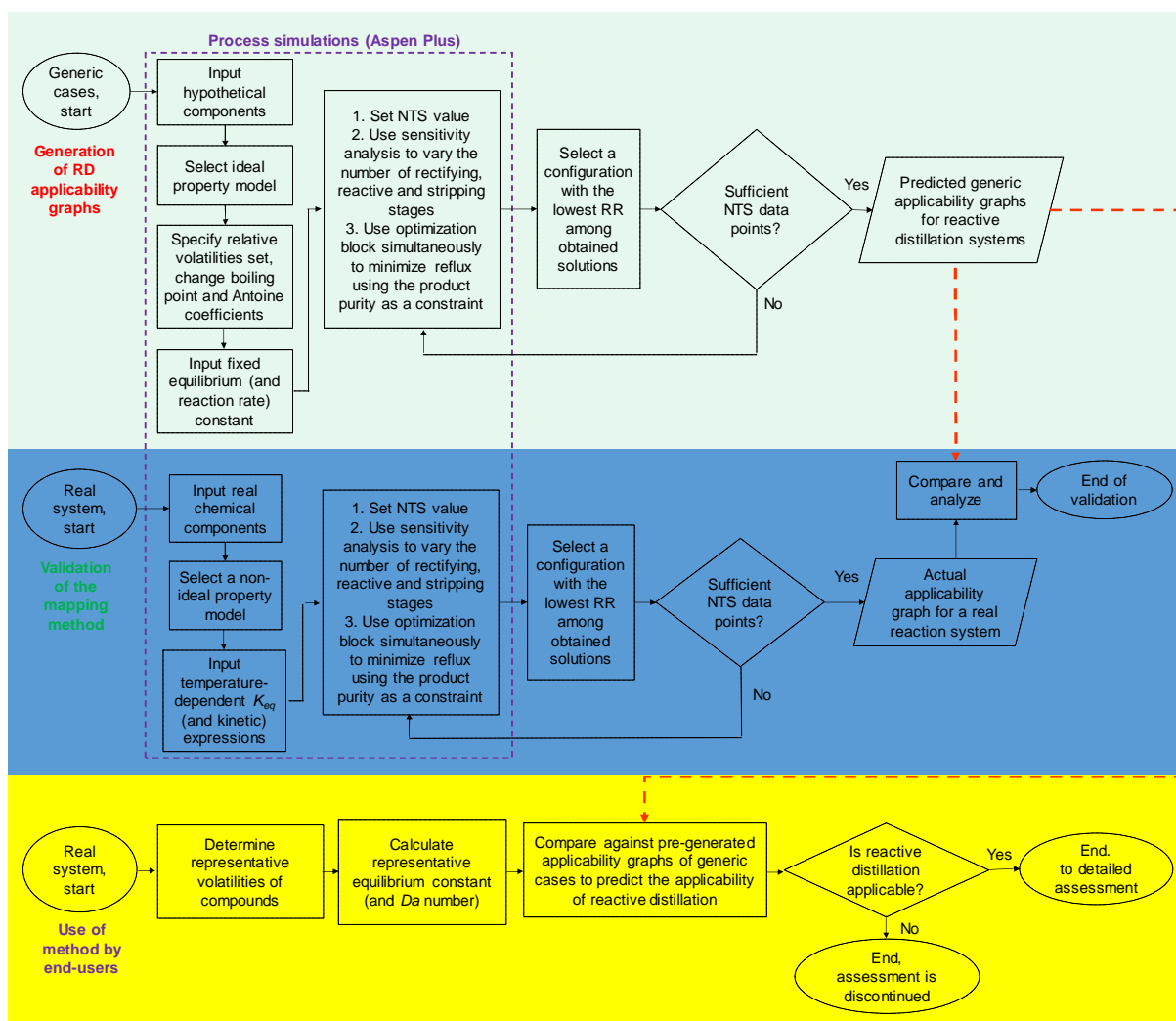
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17 **Figure 2.** (a) An illustrative applicability graph of reactive distillation and (b) an illustrative  
18 prediction of the applicability of reactive distillation to a reaction system, based on generic  
19 cases – the actual boundary line is predicted to be within the shaded area.

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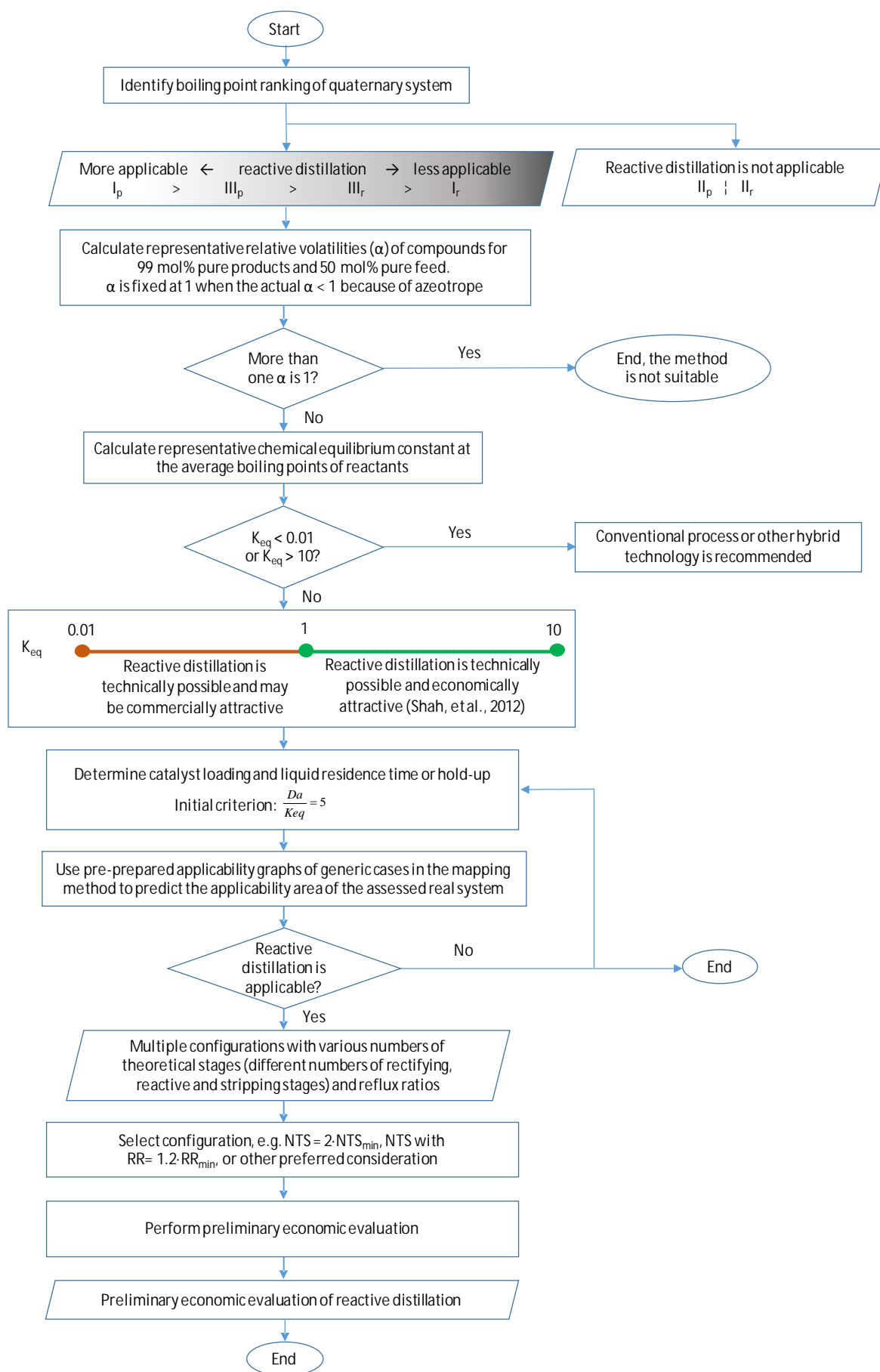
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3 **Figure 3.** Methodology developed for the generation of the applicability graphs of reactive  
 4 distillation, the validation of the mapping method and the use of the method by end-users.

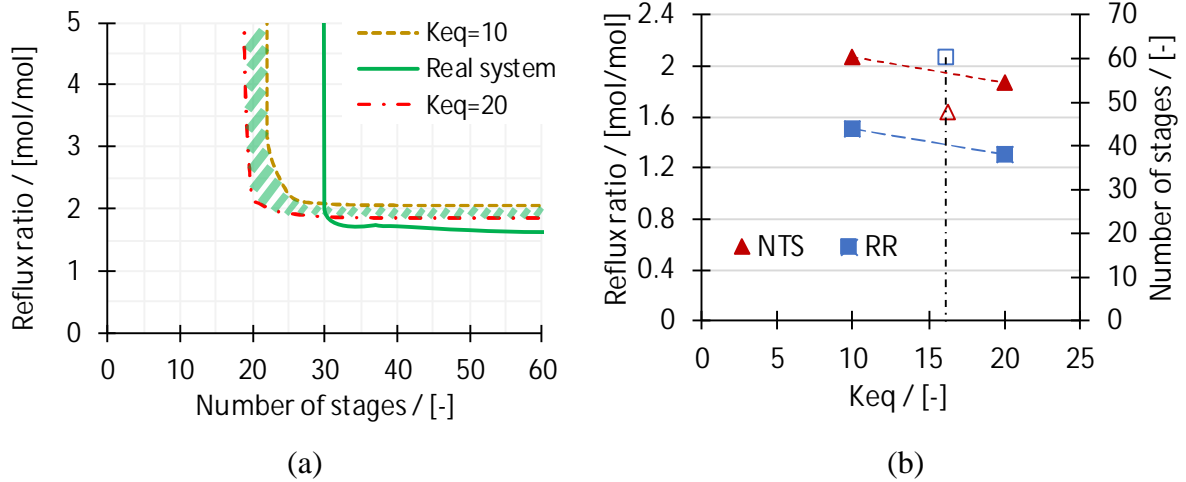
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**Figure 4.** Systematic framework for assessing the applicability of reactive distillation.

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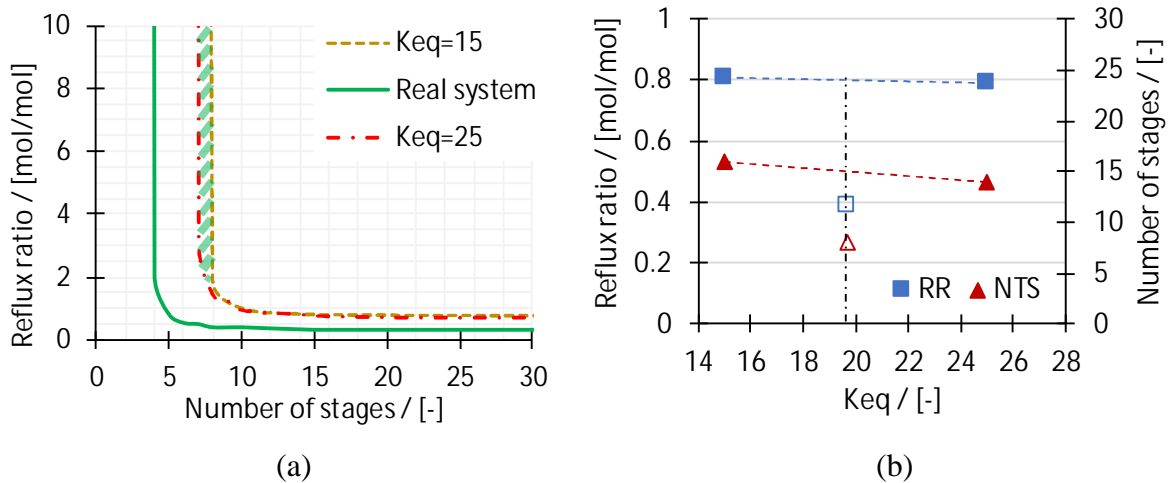
4 **Figure 5.** Case 1 – methyl acetate production via esterification (a) The predicted boundary  
 5 line of the RD applicability within the shaded area and the actual boundary line of the RD  
 6 applicability indicated by the solid line; (b) Reflux ratio and the number of theoretical stages:  
 7 solid points = estimate; open points = rigorous simulation results.

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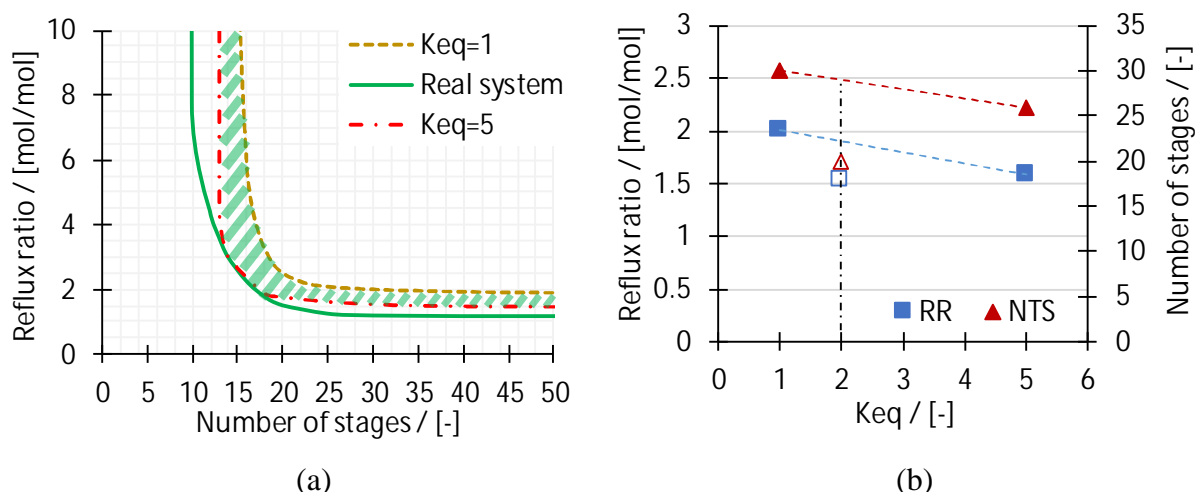


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14 **Figure 6.** Case 2 – 2-ethylhexyl acetate synthesis via esterification (a) The predicted  
 15 boundary line of the RD applicability within the shaded area and the actual boundary line of  
 16 the RD applicability indicated by the solid line; (b) Reflux ratio and the number of theoretical  
 17 stages: solid points = estimate; open points = rigorous simulation results.

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4 **Figure 7.** Case 3 – amyl acetate production via esterification (a) The predicted boundary line  
 5 of the RD applicability within the shaded area and the actual boundary line of the RD  
 6 applicability indicated by the solid line; (b) Reflux ratio and the number of theoretical stages:  
 7 solid points = estimate; open points = rigorous simulation results.

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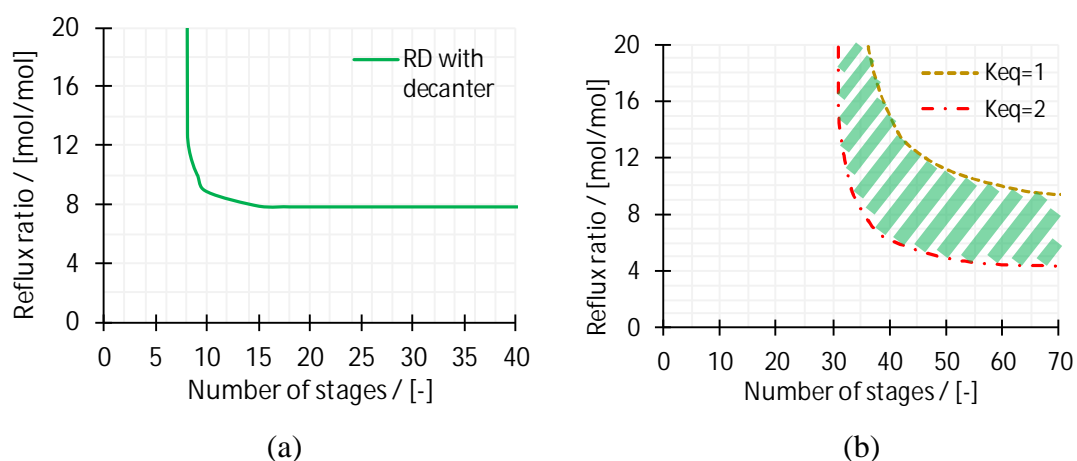
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16 **Figure 8.** (a) The actual boundary line of the applicability area of case 4 – butyl acetate  
 17 synthesis via esterification – for a heterogeneous reactive distillation setup and (b) the  
 18 predicted boundary line of the applicability area of case 5 – transesterification of methyl  
 19 acetate and butanol – within the shaded area.

## Supporting Information

### **A systematic workflow for assessing the applicability of reactive distillation for quaternary mixtures using a mapping method**

*Rahma Muthia<sup>1</sup>, Megan Jobson<sup>1</sup>, Anton A. Kiss<sup>1,2\*</sup>*

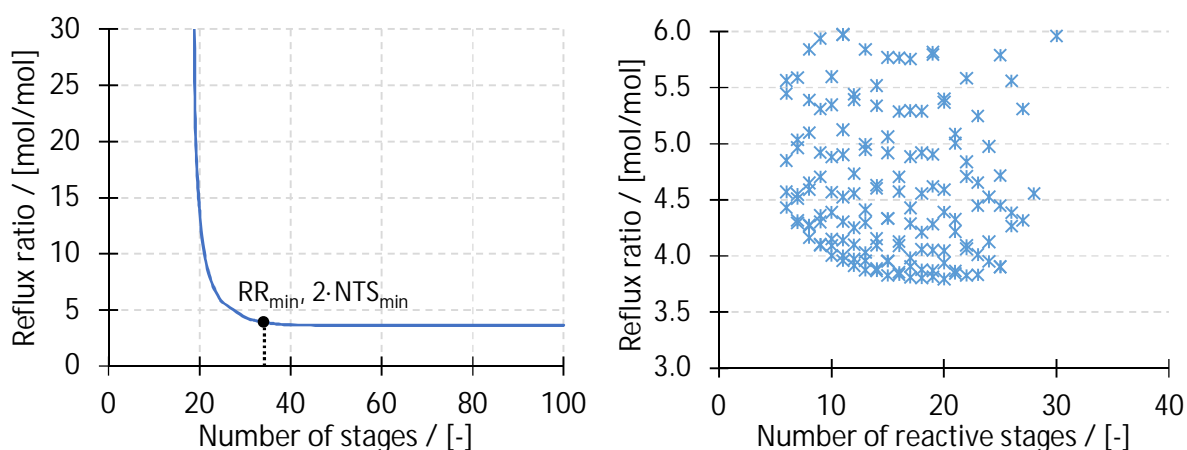
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<sup>2</sup> *Sustainable Process Technology Group, Faculty of Science and Technology, University of Twente, PO Box 217, 7500 AE, Enschede, The Netherlands*

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## 1. Multiple configurations in an applicability graph of reactive distillation

Figure S1 (a) shows the applicability graph of reactive distillation for an equilibrium-limited reaction in group I<sub>p</sub> ( $T_{b,C} < T_{b,A} < T_{b,B} < T_{b,D}$ ), considering  $\alpha_{AB} = 1.5$ ,  $\alpha_{CA} = 2$  and  $\alpha_{BD} = 2$  at  $K_{eq} = 0.1$ . The applicability graph is relevant for the product purity of  $\geq 99$  mol%. For this case,  $2 \cdot NTS_{min} = 36$ . Close to the boundary line at  $NTS = 36$ , there are multiple configurations available with various combinations of rectifying, reactive and stripping stages – their numbers of reactive stages are highlighted in Figure S1 (b). Some multiple configurations are given in details in table S1, in which within only 3% of RR change, at least there are 17 possible RD configurations.



**Figure S1.** (a) Applicability graph of equilibrium-limited reaction ( $\alpha_{AB} = 1.5$ ,  $\alpha_{CA} = 2$ ,  $\alpha_{BD} = 2$ ,  $K_{eq}=0.1$ ); (b) Number of reactive stages required for different column configurations ( $NTS = 2 \cdot NTS_{min} = 36$ ), according to the Supporting Information provided in (Muthia et al., 2018).

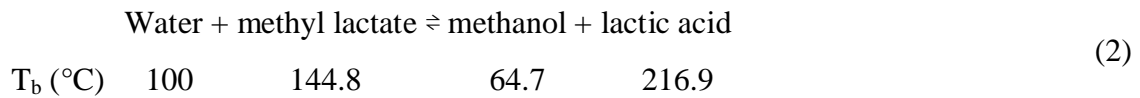
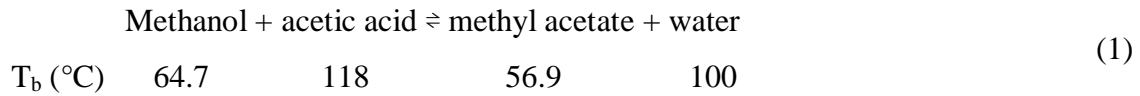
**Table S1.** Multiple column configurations for an equilibrium-limited reaction, considering ( $\alpha_{AB} = 1.5$ ,  $\alpha_{CA} = 2$ ,  $\alpha_{BD} = 2$ ,  $K_{eq} = 0.1$ ), according to the Supporting Information provided in (Muthia et al., 2018).

Number of theoretical stages	Reflux ratio	Number of rectifying stages	Number of reactive stages	Number of stripping stages
36	3.795	7	20	9
36	3.802	8	18	10
36	3.807	8	17	11
36	3.816	7	19	10
36	3.826	6	22	8
36	3.827	9	15	12
36	3.831	6	23	7
36	3.834	9	16	11
36	3.843	7	21	8
36	3.855	8	16	12

36	3.866	6	21	9
36	3.867	9	14	13
36	3.868	8	19	9
36	3.875	10	13	13
36	3.875	7	18	11
36	3.888	10	14	12
36	3.902	5	25	6

## 2. Ratio of the Damköhler number to the chemical equilibrium constant

The ratio between the Damköhler number and the chemical equilibrium constant is assessed using two case studies that represent non-ideal reaction systems – synthesis of methyl acetate and hydrolysis of methyl lactate.



The chemical equilibrium constant and the forward reaction rate constant ( $\text{mol g}_{\text{cat}}^{-1} \text{min}^{-1}$ ) relationships for the synthesis of methyl acetate are presented by Pöpken et al. (2000) as:

$$\ln(K_{eq}) = -3.82 + 2408.65 / T \quad (3)$$

$$k_f = 4.94 \cdot 10^2 \cdot \exp(-49,190 / R \cdot T) \quad (4)$$

The chemical equilibrium constant and the forward reaction rate constant ( $\text{mol g}_{\text{cat}}^{-1} \text{min}^{-1}$ ) relationships for the hydrolysis of methyl lactate are provided by Sanz et al. (2004),

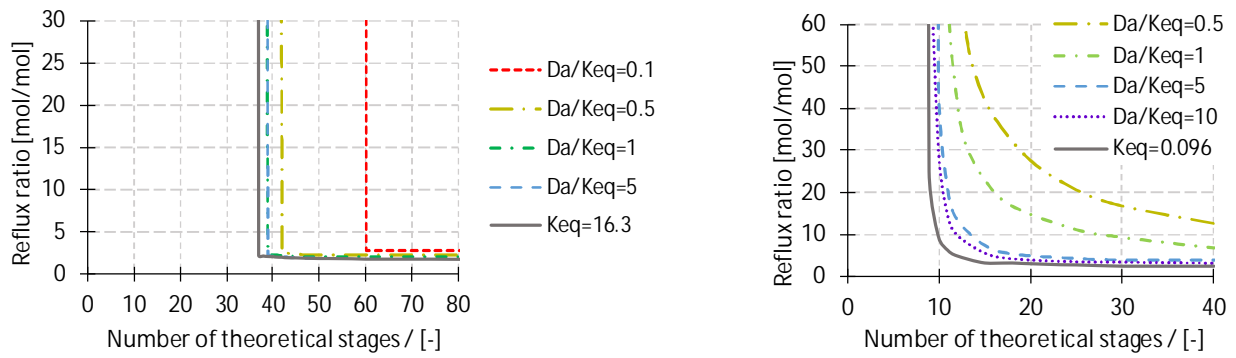
$$\ln(K_{eq}) = 2.6 - 1954.2 / T \quad (5)$$

$$k_f = 1.65 \cdot 10^5 \cdot \exp(-50,910 / R \cdot T) \quad (6)$$

In the first case, two homogeneous azeotropes exist between methyl acetate (65.9 mol%)–methanol (34.1 mol%) at 53.7°C and methyl acetate (89 mol%)–water (11 mol%) at 56.4 °C. In the second case, there is an azeotrope identified between water (97 mol%) and methyl lactate (3 mol%) at 99.8 °C.

Figure S2 shows applicability graphs for both case studies generated using rigorous simulations in Aspen Plus. It is observed that the applicability areas of both kinetically controlled and equilibrium-limited reactions are similar for  $\text{Da}/K_{eq} \geq 5$ .





**Figure S2.** Applicability graphs of reactive distillation for (a) synthesis of methyl acetate; (b) hydrolysis of methyl lactate

### 3. Preliminary economic evaluation of reactive distillation

The systematic workflow presented in this work allows engineers in the chemical industries to assess the applicability of reactive distillation, based on a mapping method that we have developed (Muthia et al., 2018, 2019a, 2019b). When reactive distillation is applicable, preliminary economic evaluation is conducted for the chosen reactive distillation configuration, by using adapted steps of cost estimation for conventional distillation. Complete procedures of economic evaluation for conventional distillation are explained elsewhere (Douglas, 1998; Seider et al., 2010; Towler and Sinnott, 2012).

Total annualized cost (TAC) is a key variable to compare the reactive distillation process with other conventional or hybrid systems. It comprises two elements: annualized investment cost (AIC) defined as the total investment cost (TIC) relative to pay-back period (PBP), and total operating cost (TOC). The components of AIC include the costs of column shell and internals, condenser, reboiler, reflux drum and any additional equipment (e.g. pumps). TOC include the costs of cooling water, steam and catalyst. Eqs. (1)-(5) present some important cost correlations for TAC, TIC and TOC (Douglas, 1998), where costs are updated from 1998 (Marshall and Swift index, M&S = 280) to the current year using the current value of the M&S index (M&S = 1638.2 at the end of 2018).

$$TAC = \frac{TIC}{PBP} + TOC \quad (7)$$

$$TIC_{RD,Shell} = \left( \frac{M \& S}{280} \right) \cdot 101.9 \cdot D^{1.066} \cdot H^{0.802} \cdot (2.18 + F_C) \cdot F_{lang} \quad (8)$$

$$TIC_{RD,Internal} = \left( \frac{M \& S}{280} \right) \cdot 4.7 \cdot D^{1.55} \cdot H \cdot F_c \cdot F_{Lang} \quad (9)$$

$$TIC_c = \left( \frac{M \& S}{280} \right) \cdot 101.3 \cdot A_c^{0.65} \cdot (2.29 + F_c) \cdot F_{Lang} \quad (10)$$

$$TIC_r = \left( \frac{M \& S}{280} \right) \cdot 101.3 \cdot A_r^{0.65} \cdot (2.29 + F_c) \cdot F_{Lang} \quad (11)$$

$A_c$	: Heat-transfer area for condenser
$A_r$	: Heat-transfer area for reboiler
$D$	: Diameter of reactive distillation column (m)
$F_c$	: Correction factor of total of investment cost
$F_{Lang}$	: Lang factor (ref)
$H$	: Height of reactive distillation column (m)
$M\&S$	: Marshall & Swift equipment cost indexes (ref)
$PBP$	: Pay-back period (years)
$TAC$	: Total annual cost (\$/y)
$TIC$	: Total investment cost (\$)
$TIC_{RD,Internal}$	: Total investment cost for internals of reactive distillation column (\$)
$TIC_{RD,Shell}$	: Total investment cost for shell of reactive distillation column (\$)
$TOC$	: Total operating cost (\$/y)

#### 4. Calculations of representative relative volatilities of compounds

Eq. (6) defines the relative volatility of  $i$  and  $j$  in terms of the liquid and vapour mole fractions ( $x$  and  $y$ ) at phase equilibrium:

$$\alpha_{ij} = \frac{K_i}{K_j} = \frac{\left( \frac{y_i}{x_i} \right)}{\left( \frac{y_j}{x_j} \right)} \quad (6)$$

Tables S2-S6 provide the compositions of mixtures in vapor and liquid phases for 99 mol% pure products and 50 mol% pure reactants. The data given is applied at atmospheric pressure and it is assumed that the stream is at saturated conditions (i.e. liquid at boiling point).

**Table S2.** Case 1: Vapor and liquid compositions of mixtures (methyl acetate production via esterification)

Feed composition	$y_i$	$x_i$	$y_j$	$x_j$	$K_i$	$K_j$	$\alpha_{ij}$
99 mol% of methyl acetate (i) 1 mol% of methanol (j)	0.98	0.99	0.02	0.01	0.99	1.92	0.52
50 mol% of methanol (i) 50 mol% of acetic acid (j)	0.86	0.50	0.14	0.50	1.73	0.27	6.28
1 mol% of acetic acid (i) 99 mol% of water (j)	0.006	0.01	0.99	0.99	0.60	1.00	1.66

**Table S3.** Case 2: Vapor and liquid compositions of mixtures (2-ethylhexyl acrylate synthesis via esterification)

Feed composition	$y_i$	$x_i$	$y_j$	$x_j$	$K_i$	$K_j$	$\alpha_{ij}$
99 mol% of water (i) 1 mol% of acrylic acid (j)	0.99	0.99	0.006	0.01	1.00	0.62	1.63
50 mol% of acrylic acid (i) 50 mol% of 2-ethylhexanol (j)	0.80	0.50	0.20	0.50	1.60	0.40	3.96
1 mol% of 2-ethylhexanol (i) 99 mol% of 2-ethylhexyl acrylate (j)	0.05	0.01	0.95	0.99	5.04	0.96	5.25

**Table S4.** Case 3: Vapor and liquid compositions of mixtures (amyl acetate production via esterification)

Feed composition	$y_i$	$x_i$	$y_j$	$x_j$	$K_i$	$K_j$	$\alpha_{ij}$
99 mol% of water (i) and 1 mol% of acetic acid (j)	1.00	0.99	0.005	0.01	1.00	0.52	1.95
50 mol% of acetic acid (i) and 50 mol% of amyl alcohol (j)	0.63	0.50	0.37	0.50	1.27	0.73	1.73
1 mol% of amyl alcohol (i) and 99 mol% of amyl acetate (j)	0.018	0.01	0.98	0.99	1.80	0.99	1.82

**Table S5.** Case 4: Vapor and liquid compositions of mixtures (n-butyl acetate synthesis via esterification)

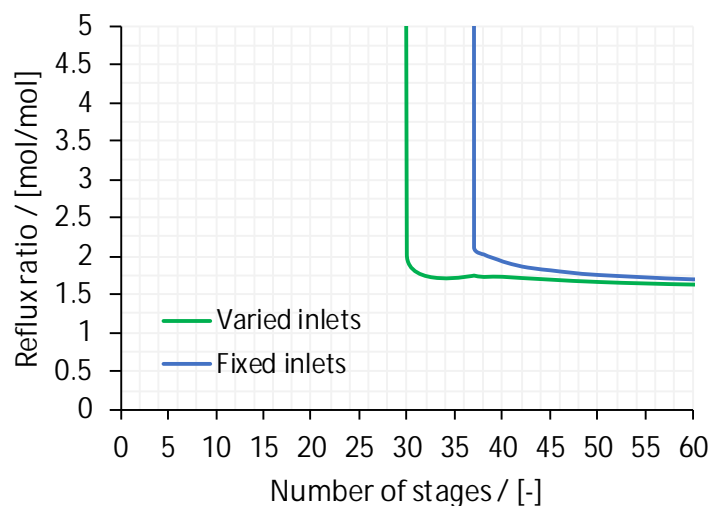
Feed composition	$y_i$	$x_i$	$y_j$	$x_j$	$K_i$	$K_j$	$\alpha_{ij}$
99 mol% of water (i) and 1 mol% of acetic acid (j)	0.99	0.99	0.007	0.01	1.00	0.70	1.42
50 mol% of acetic acid (i) and 50 mol% of n-butanol (j)	0.49	0.50	0.51	0.50	0.98	1.02	0.95
1 mol% of n-butanol (i) and 99 mol% of n-butyl acetate (j)	0.98	0.99	0.02	0.01	0.99	1.75	0.57

**Table S6.** Case 5: Vapor and liquid compositions of mixtures (transesterification of methyl acetate and n-butanol)

Feed composition	$y_i$	$x_i$	$y_j$	$x_j$	$K_i$	$K_j$	$\alpha_{ij}$
1 mol% of methyl acetate (i) and 99 mol% of methanol (j)	0.03	0.01	0.97	0.99	3.29	0.98	3.37
50 mol% of methyl acetate (i) and 50 mol% of n-butanol (j)	0.92	0.50	0.08	0.50	1.85	0.15	12.0
1 mol% of n-butanol (i) and 99 mol% of n-butyl acetate (j)	0.02	0.01	0.98	0.99	1.84	0.99	1.85

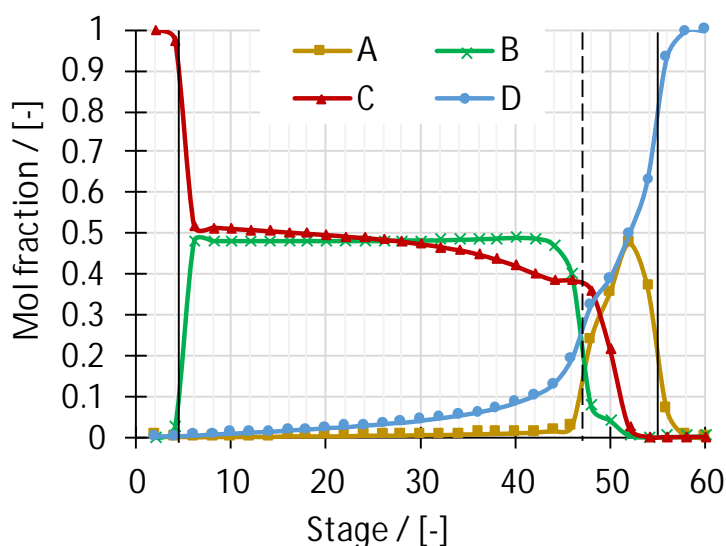
## 5. Applicability assessment of Case 1 (methyl acetate production via esterification)

The position of feed stages within the reactive zone notably affects the size of the applicability graph of case study 1, as an immediate contact between reactants contributes to minimize the formation of azeotrope between reactant and product. Figure S2 presents the applicability graphs of reactive distillation for fixed feed stages at the top and the bottom stages of the reactive zone and varied feed stages within the reactive zone.



**Figure S3.** Applicability graphs of Case 1 obtained from rigorous simulations

Figure S3 shows the composition profile of a column configuration (2 rectifying, 51 reactive and 7 stripping stages, and reflux ratio of 1.8) that exists close to the boundary line of the applicability graph for Case 1. The high chemical equilibrium constant of this system ( $K_{eq} = 16.3$  at  $91.4^{\circ}\text{C}$ ) allows a high conversion of reactants in the reactive section of the column. In this system classified into group III<sub>p</sub> ( $T_{b,C} < T_{b,A} < T_{b,D} < T_{b,B}$ ), it is crucial to prevent reactant B from reaching the stripping section, as it is the heaviest component that could interfere the high purity of product D.



**Figure S4.** The composition profile of a column configuration for Case 1. The solid vertical lines depict the start and end of reactive section. The dashed line is the feed stage of reactant A, while the feed stage of reactant B overlaps with the start of reactive section.

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