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Process integration and control tied to economic optimization in biobutanol synthesis

Integración de procesos y control ligado a la optimización económica en la síntesis de biobutanol

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Dedicatory

To my Family.

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Resumen

Diferentes esquemas de destilación con integración de calor y de fermentación-separación fueron propuestos, y evaluados para la producción de butanol o etanol en el ambiente de simulación. Los requerimientos de combustible de los esquemas propuestos en este trabajo están entre los más bajos encontrados en la literatura para la producción de butanol y etanol. Esquemas de destilación doble-efecto o integración de calor de columnas de alta y baja presión son la opción más económica de separación externa, con requerimientos energéticos entre 30 y 50% más bajos que los sistemas convencionales. Los reactores integrados con separación alcanzaron requerimientos energéticos totales mayores a los sistemas de destilación con integración de calor. La configuración más rentable para la producción de acetona, butanol y etanol a partir de lignocelulosa fue seleccionada después de la optimización de cada uno de los procesos. Un sistema de reacción con extracción simultánea por alcohol oleico de los inhibidores producidos en el pretratamiento y en la fermentación, fue la opción más económica de producción a partir de lignocelulosa. Las condiciones óptimas de operación del proceso con extracción fueron seleccionadas a partir de la maximización del potencial económico con perturbaciones. De esta manera, el proceso fue estable a condiciones económicas óptimas.

Palabras clave: Optimización; intensificación de procesos; destilación; fermentación ABE; modelo cinético

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Abstract

Several heat integrated distillation systems were proposed and evaluated for the separation of butanol and ethanol on simulation environment. The fuel requirements of these systems are among the lowest found in the literature for butanol production. Double-effect distillation systems are the most economical choice of external separation, with energy requirements 30-40% lower than that for distillation systems without recovery of condensation heat. The best configuration for the production of acetone, butanol and ethanol (ABE) was selected by optimization. A rigorous kinetic model for ABE production was developed and used in the simulations. Integrated reactor with separation units reached total energy requirements higher than external separation schemes with heat integration. However, integrated reactors were economically preferable because they reduce the water consumption and the size of the reactor for three and two-fold, respectively. A simultaneous reaction system with detoxification of inhibitor from pretreatment was the low-priced option for ABE production from lignocellulose. The optimal operating conditions of the system were selected to facilitate the process control at economic optimal conditions.

Keywords: optimization, process integration, distillation; ABE fermentation; kinetic model

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Introduction

The butanol is used in the manufacture of resins, pharmaceuticals, plasticizers and synthetic ester; and it is considered an alternative biofuel [1]. As a biofuel, biobutanol can be blended with gasoline in higher ratios than bioethanol, and it is less corrosive and has a lower heating value [2]. N-butanol is chemically produced from propylene in the oxo process (with H_2 and CO over rhodium catalyst), aldol process from acetaldehyde, biomass gasification, catalysis Guerbert (condensation of ethanol) and by fermentation [3]. Butanol production by fermentation was the second largest in the world before 1950 [4]. However, fermentation process was not profitable with the emergence of the petrochemical production [4]. In recent years, oil prices and growing concerns about global warming have renewed interest in the biotechnological production [1,5]. In order to improve the economics of fermentation process, various processes have been developed:

Alternative microorganisms

In conventional fermentation, mainly butanol, ethanol, and acetone are produced. For this reason, it is known as ABE fermentation. This fermentation is carried out by various types of solvent-producing clostridia (*C. acetobutylicum, C. saccharobutylicum, C. butylicum, C. beijerinckii*) [6]. In the ABE fermentation, due to the high toxicity of butanol, ABE yields are achieved near to 33 %, productivities lower than 0.5 g-ABE $L^{-1}h^{-1}$ and ABE concentrations less than 2% [7]. Butanol can be produced inserting genes of *Clostridium* in unconventional strains as *Escherichia coli* [8–13], *Pseudomonas putida* [14,15], *Bacillus subtilis* [15,16], *Lactobacillus brevis* [17,18] and *S. cerevisiae* [19]. Unconventional strains produce only butanol at concentrations below 2% [5,9,20]. Raising the concentration of butanol is a key aspect of the energy efficiency of the process. For example, studies of butanol separation by distillation, indicate that if the butanol concentration is increased from 10 to 40 gL^{-1}, the fuel requirement for separation is reduced in 80 % [21]. Non-native strains can also produce only isobutanol [5]. The isobutanol is an attractive biofuel but cannot to supply the chemical market of n-butanol [5,22].

Alternative substrates

Clostridium can consumes sucrose, fructose, glucose, glycerol, mannose, lactose, dextrin, starch, glycerol, pentoses (xylose, arabinose) and inulin [4,7]. In a conventional corn-based plant, substrate represents up to 78% of the cost of production, while energy on operations, including distillation, contributes 14% of total cost [5]. Therefore, the transition towards cheaper feedstocks offers the biggest opportunity for cost saving. In the literature, several substrates have been studied by biobutanol production: Organic domestic waste water [23,24], apple pomace [25], wheat straw [26], damaged corn [27], barley straw [28], peanut [29], potatoes [30], Jerusalem artichoke [31], corn stover [28,32,33], dried distillers grains with solubles (DDGS) [31].

Acid supplementation in ABE fermentation

The metabolism of solventogenetic clostridia occurs in two stages, in the first, is carried out the acid production and cell growth; in the second, acids are consumed and solvent production begins [4]. The addition of acetic, lactic and butyric acids has been studied to improve the performance, productivity, and solvent concentration. Acetic acid increases the yield of solvents [34]. Butyric acid inhibits its production and increases the butanol production [35]. Feeding of lactic acid increases the product concentration, yield, and productivity of butanol [36]. For this reason, two-stages reactor for the butanol production has been proposed in the literature [37]. In the first reactor, butyric acid production is given by *Clostridium tyrobutyricum* and in the second, the acids are converted by a strain solventogenetic. In a reactor with cell immobilization and butyric acid supplementation a butanol yield of 42%, ABE yield of 0.52, volumetric productivity of 4.6 $gL^{-1}h^{-1}$ and butanol concentration of 5.1 gL^{-1} [38] was obtained.

Immobilization o cell recycle

Increasing productivity is essential to reduce the total investment. For example, if productivity is increasing in two times capital investment is reduced by 20% [5]. For this reason, has been proposed immobilization or cell recirculation [39–44]. With cell recycle or immobilization has been able to increase reactor productivity between 16 and 30 times [39–44]. In this type of reactor inhibition and toxicity caused by butanol is not limited, so it must be fed a diluted substrate (<60 gL^{-1}). Solids in the feed must be removed. Reduction of the cost of the reactor should be less than the cost of the units used for recirculation.

Integrated reactors with separation units

In fermentation systems with selective separation of butanol product inhibition and toxicity on the microorganism are reduced [7]. Thus, in integrated reactors productivity and product concentration are increased [7]. Additionally, can be used a more concentrated substrate, reducing water consumption and the consequent vinasse production. In the literature, there have been proposed different fermentation systems integrated with gas-striping [45–47], pervaporation [48–55], liquid-liquid extraction [56–62], pertraction [63], adsorption [40] and flash evaporation [64,65].

Groot et al. [66] reported that the pervaporation was the technique with less energy consumption (9 MJ/Kg de ABE). Qureshi et al. reported that pervaporation was third with lower requirements with 14 MJ/Kg. Qureshi et al. [67] reported that the extraction and adsorption were the most energy efficient techniques, with heat recoveries of 8.2 MJ/Kg. The divergence between the results achieved in energy assessments is generated by the simplifications of the simulation; selectivity of separation agent and systems. A detailed economic, energy and environmental comparison of different recovery techniques are still needed to establish the best reaction and separation system [5].

Patents in biobutanol separation

Several patents have been developed for efficient biobutanol production [68–77]. Kaufman et al. [74] proposed a distillation system with multistage compression. In this system, condensation heat is used to apply heat at its boiler. Therefore, the energetic requirement is given by compression work. Ollivier et al. [75] develop an integrated reactor with gas stripping. CO_2 is is recirculated after of feeding in column stripping to solvent recovery. Frank et al. [72] proposed a hybrid system using vacuum distillation without reflux. This is a process better than an integrated reactor with vacuum evaporation because a more concentrated product is achieved with a less energetic requirement. Evanko et al. [71] patent a system for biobutanol purification by azeotropic distillation, using decantation after each stage of distillation. Grady et al. [73] proposed a distillation system for recovery of butanol of an organic extractant. Volatile hydrocarbons are feeding in the top, as hexane, for facilitated butanol purification and extractant regeneration.

Process control and economic optimization

Mariano et al. [64] proposed a dynamic study and studied strategies of control by ABE fermentation in a hybrid system with vacuum evaporation. The control algorithm used was the dynamic matrix control (DMC). The control strategies implemented are performed using the method "single input/single output" (SISO) or "multiple input/multiple outputs" (MIMO). Comparison with conventional PI control is performed. The control is studied for diminishing the strong effect in the fermentation of fluctuations in substrate concentrations and to maintain the equilibrium liquid-vapor before perturbations in the temperature of fermentation. PI performance was superior in ratio to DMC because it show a quicker response without oscillations. Luyben [78] studied the control of an azeotropic distillation system using the software Aspen Plus ®. In this work, a PI control was sufficiently robust for this system. Oudshoorn [79] proposed a short-cut method for analysis economical of integrated systems for production of bio-bulk chemicals. However, economical optimization was not studied. Others studied of control or optimization has been reported until this moment in searches or databases ACS, Elsevier, Wiley Online Library, Springerlink and google scholar.

Thesis structure

The evaluation of integrated systems for biobutanol production was studied in this work on simulation environment using the software's Matlab 2015b and Aspen Plus 7.3V®. Thermodynamic parameters for UNIQUAC liquid-liquid equilibrium were adjusted. A kinetic model was proposed for biobutanol production using lignocellulose substrate. In the first chapter, was proposed several heat integrated distillation systems for exclusive isobutanol production. The energetic analysis was performed in fuel equivalent, therefore, energetic results are proportional to CO_2 emissions. Comparison of butanol with ethanol separation in heat integrated systems was performed because is the current main biofuel.

In the second chapter, several heat integrated distillation systems were proposed for ABE separation. A distillation system of 4 columns, using dual-effect and low-high-pressure columns was the option more profitable. Energetic and economical evaluation of biocatalysts with the highest concentrations of ABE were studied. In the third chapter, an alternative extractant regeneration system was compared with several external extraction systems, because extractive fermentation was the most profitable process. In the fourth chapter, an integrated reactor with pervaporation and vacuum evaporation was optimized rigorously. In the five chapter, an integrated reactor and efficient detoxification system with liquid-liquid extraction was proposed and optimized. In the six chapter, the stability of this reactor was studied.

1. Ethanol and isobutanol dehydration by heat-integrated distillation

Abstract

Alternative processes with double-effect distillation (DED) and vapor compression distillation (VCD) were studied for ethanol and isobutanol dehydration from dilute concentrations. The extractants evaluated for ethanol dehydration were glycerol and ethylene glycol. Simulations were performed in Aspen Plus®. The lowest energy consumption for ethanol and isobutanol dehydration were achieved by VCD (2.5 and 3.7 MJ-fuel/kg-product, respectively). The energy consumption for isobutanol and ethanol separations with VCD were 25-30% and 39-40% lower than DED, respectively. Due to the high cost of the compressors, VCD was between 6 and 16% more expensive than DED. Due to the higher ethanol concentration from the fermentation broth, the separation annualized costs and the fuel requirement for ethanol dehydration were 43-47% and 32-46% lower than butanol separation, respectively. However, the energy efficiency for isobutanol and ethanol processes, with a maximum theoretical yield from glucose, was approximately equivalent, 72-73% (DED) and 77% (VCD), due to the higher combustion heat of isobutanol.

Keywords: extractive distillation; double-effect distillation; vapor compression distillation; biobutanol; bioethanol

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Abbreviations

DED, Double-effect distillation	TOAC, total operational annualized cost
LHV, lower heating value	VCD, vapor compression distillation
PRE, pre-concentration column	S-I, isobutanol dehydration process with VCD
TAC, total annualized cost	S-II, isobutanol dehydration process with DED
TAIC, total annualized investment cost	S-III, ethanol dehydration process with VCD
TED, extractive column	S-IV, ethanol dehydration process with DED
TER, column for extractant regeneration	

1.1. Iintroduction

Bioethanol from sugar and grains is the dominant biofuel in the market. Isobutanol, an alternative biofuel, has higher energy content, lower vapor pressure and lower corrosivity than ethanol [80]. Industrially, butanol and ethanol separation are carried out mainly by distillation [78,81]. Distillation is the unit of most energy consumption in the process [82]. Therefore, this work studied alternatives of distillation with low energy consumption for isobutanol and ethanol production.

Butanol is mainly produced via petrochemical [80]. Biotechnological production of butanol is carried out conventionally by acetobutylic fermentation. In this fermentation, acetone and ethanol are obtained as by-products. Low butanol concentration (< 2 wt%) cause high toxicity and high product inhibition in biocatalyst [83]. Consequently, acetobutylic fermentation has low productivity, expensive energy consumption, and low yield [80]. Alternatively, recombinant microorganisms have been developed for exclusive production of isobutanol [5,84,85]. *Escherichia coli, Saccharomyces cerevisiae*, and *B. subtilis* are the most well studied microbial strains that can be potentially induce to the butanol production [84]. In these fermentation processes, isobutanol is produced at concentrations lower than 2 wt% [5].

Several integrated reactors with gas stripping, pervaporation, liquid extraction or adsorption have been proposed in the literature to avoid high butanol toxicity [86–92]. In these systems, reactor productivity and the final biobutanol concentration are increased. Final separation of this process is carried out by azeotropic distillation. Water-butanol azeotrope behavior is broken by decantation. The energy requirements of an integrated reactor depend of both, the distillation and the separation units of hybrid systems. Therefore, a distillation efficient system is necessary to improve the performance of integrated reactors.

Ethanol in contrast to isobutanol is produced principally by fermentative route. Wine obtained after fermentation contains about 7-12 wt% of ethanol. Due to azeotrope known at 95.3 wt%, an entrainer is necessary in bioethanol purification. Several process have been proposed for ethanol dehydration such as molecular sieves [93], membranes [94], azeotropic distillation [95], extractive distillation [96–99] or hybrid methods combining these options [94,95,100]. The extractive distillation is one of the most economical ways to produce anhydrous ethanol [101].

Process intensification in distillation follows various integration routes such as: internal heat integrated distillation columns (HIDiC) [102,103], vapor compression distillation (VCD) [74], petlyuk or dividing wall columns [104,105] and double-effect distillation (DED) [106–108]. Dividing wall and petlyuk distillation are used with more than two components. Hence, it is not useful for isobutanol separation. In DED, the fed flow is divided and pumped into the two distillation columns. One column operates at low pressure and the other at atmospheric pressure or higher. In such a way that the condensation heat of the higher pressure column can be used to supply heat to the boiler of vacuum pressure column. In VCD, the vapor of top in the column is compressed to supply the condensation heat to its reboiler.

DED [107] and VCD [109] have been studied to obtain hydrous ethanol (93 wt%). VCD with extractive distillation was studied in dividing wall scheme [110–112]. In butanol dehydration, multistage VCD was proposed by ABE separation in Cobalt technologies® patent [74]. In this work heat-integrated distillation with VCD and DED were studied by ethanol and isobutanol dehydration. Extractive distillation for ethanol dehydration was studied in this work. Both integrated process, VCD and DED, involve more capital investment than conventional separation. Therefore, an economic study was performed.

1.2. Methodology

TOAC, TIAC, PP and F_p, ta, were operating costs, capital investment, payback period (3 years), product flow, and annual operation time (8150 h) respectively. Costs of steam, cooling water and electricity were assumed as 16.3 \$/kg, 0.0067 \$/kg, and 0.086 \$/kWh respectively. Glycerol cost was 3 \$/kg. The Marshall & Swift equipment cost index (M&S) has a value of 1569[113]. Process equipment were designed using stainless steel material. Energy requirement was calculated with an efficiency steam and electricity production from fuel of 0.9 and 0.3 respectively. The simulation conditions were determined with an energetic minimization in Aspen Plus®.

The distillation columns were simulated with RadFrac using the software Aspen Plus®. The property method for equilibrium liquid vapor was NRTL-HOC. UNIQUAC-LL parameters from Aspen Plus ® were used to simulate the decanter in isobutanol separation. Ethanol and isobutanol recovery by distillation process were fixed in 99.8%. The columns were simulated with Murphree efficiencies of 0.7. In the simulation, sieve trays were assumed. Diameter and pressure drop was calculated with Aspen Plus® tool. The spacing plate was fixed at 0.61 m. Compressors were simulated with an isentropic efficiency of 0.75. Heat integration was realized with 10 ºC of minimum approach temperature. In all cases tested, vinasses were used for preheating the feed. The purity of solvent was 0.997. Total annualized cost (TAC) was calculated by Guthrie method [114]:

$$TAC = \frac{TOAC + {}^{TIAC}\!/_{t_{ri}}}{F_p \cdot t_a} \tag{1-1}$$

TOAC, TIAC, PP, and F_p, ta, were total operation annualized costs, total capital annualized investment, payback period (3 years), product flow, and annual operation time (8150 h), respectively. Costs of steam, cooling water and electricity were assumed as 16.3 \$/kg, 0.0067 \$/kg, and 0.086 \$/kWh, respectively. Glycerol cost was 3 \$/kg. The Marshall & Swift equipment cost index (M&S) has a value of 1569 [113]. Process equipment was designed using stainless steel material. Energy requirement was calculated with an efficiency in steam and electricity production from fuel of 0.9 and 0.3, respectively. The simulation conditions were determined by an energetic minimization in Aspen Plus®.

1.2.1. Description of process for isobutanol dehydration

Isobutanol final purification is conventionally carried out in two steps of distillation (Fig. 1-1). Although isobutanol has a boiling point higher than water, the presence of an azeotrope of the minimum boiling point allows to obtain isobutanol to compositions close to azeotropic (65.6 wt%) in the pre-concentration column (C1). Water/isobutanol azeotrope was broken in a decanter. The organic phase was fed on top of depletion column (C2). Isobutanol (99.9 wt%) was obtained in the bottoms of column C2. Aqueous phase was recirculate on top of column C1. The feed flow was pumped to stage 3 of column C1 when the isobutanol concentration in feed flow was lower than 6.5 wt%. Otherwise, the feed flow was directly pumped to the decanter.

System I (S-I) combined VCD with high-pressure distillation (Fig. 1-2). The column C1, see Fig. 2, was integrated with vapor compression. The column C2 operates at a pressure required for supply its condensation heat to reboiler of column C1. The condensation heat of column C2 in some cases, depending the concentration of feed flow, was higher than column C1 boiler requirement. In these cases, the excess of steam in the top of column C2 was compressed to supply heat to its reboiler. The trays number of columns C1 and C2 were 26 and 10, respectively. The total energy consumption of process included compressor power and the steam of the reboilers of columns C1 and C2.

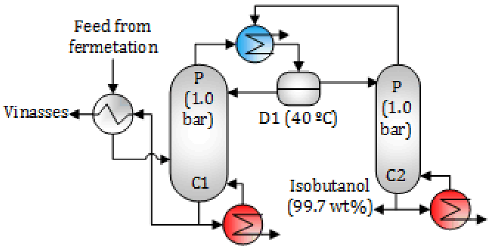


Figure 1-1. Isobutanol separation by conventional distillation

The system II (S-II) was a less intensive energetic integration choice than S-I and it had three distillation columns. The feed flow was divided and pumped to columns C1-LP and C1-HP (Fig. 1-3). Colum C1-LP was operated to 0.4 atm, and column C1-HP to 1 atm. Column C2 was used to obtain butanol of high purity (99.7 wt%). The condensation heat of columns C1-HP and C2 were used to provide heat to reboiler of C1-LP (Fig. 3). Columns C1-LP, C1-HP, and C2 had 26, 26 and 10 trays, respectively. Net fuel consumption was the sum of reboiler heat of C1-LP and C2.

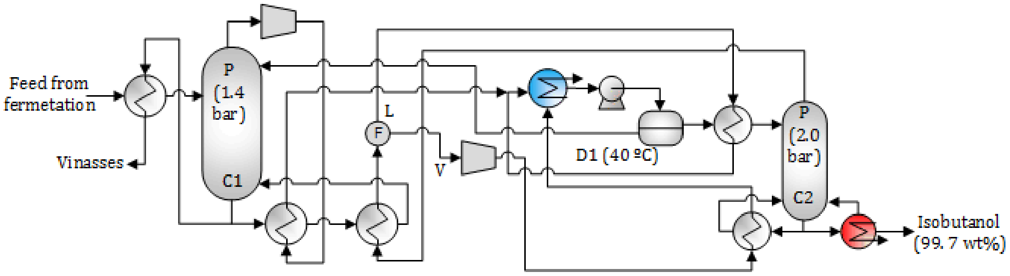


Figure 1-2. Scheme proposed of integrated distillation vapor compression for isobutanol dehydration (S-I)

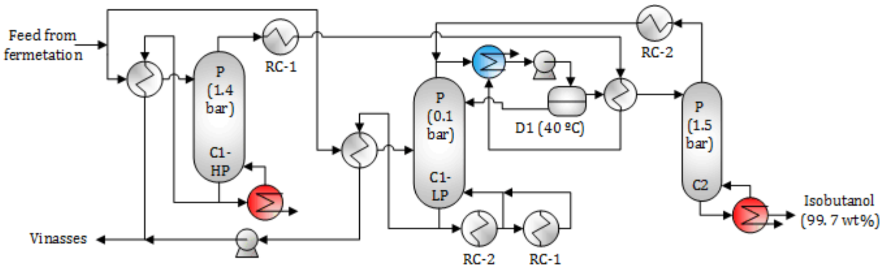


Figure 1-3. Scheme proposed by isobutanol separation with double-effect distillation (S-II)

1.2.2. Ethanol dehydration by extractive distillation systems

Isobutanol final purification is conventionally carried out in two steps of distillation (Fig. 1-1). Although isobutanol has a boiling point higher than water, the presence of an azeotrope of the minimum boiling point allows to obtain isobutanol to compositions close to azeotropic (65.6 wt%) in the pre-concentration column (C1). Water/isobutanol azeotrope was broken in a decanter. The organic phase was fed on top of depletion column (C2). Isobutanol (99.9 wt%) was obtained in the bottoms of column C2. Aqueous phase was recirculate on top of column C1. The feed flow was pumped to stage 3 of column C1 when the isobutanol concentration in feed flow was lower than 6.5 wt%. Otherwise, the feed flow was directly pumped to the decanter.

System I (S-I) combined VCD with high-pressure distillation (Fig. 2). The column C1, see Fig. 2, was integrated with vapor compression. The column C2 operates at a pressure required for supply its condensation heat to reboiler of column C1. The condensation heat of column C2 in some cases, depending the concentration of feed flow, was higher than column C1 boiler requirement. In these cases, the excess of steam in the top of column C2 was compressed to supply heat to its reboiler. The trays number of columns C1 and C2 were 26 and 10, respectively. The total energy consumption of process included compressor power and the steam of the reboilers of columns C1 and C2.

Process S-II was a less intensive energetic integration choice than S-I and it had three distillation columns. The feed flow was divided and pumped to columns C1-LP and C1-HP (Fig. 3). Colum C1-LP was operated to 0.4 atm, and column C1-HP to 1 atm. Column C2 was used to obtain butanol of high purity (99.7 wt%). The condensation heat of columns C1-HP and C2 were used to provide heat to reboiler of C1-LP (Fig. 3). Columns C1-LP, C1-HP, and C2 had 26, 26 and 10 trays, respectively. Net fuel consumption was the sum of reboiler heat of C1-LP and C2.

The conventional extractive distillation (C-I) was simulated in three stages (Fig. 4). In the first column (TPC), ethanol was pre-concentrated. In the extractive column (TED), ethanol anhydrous was obtained using glycerol or EG as entrainer. In the column TER, extractant was regenerated (Fig. 1-4). TPC, TED, and TER were designed with a total of trays of 25, 17 and 10, respectively. Dilute solutions were fed to TPC in the stage 9. Glycerol of high purity and ethanol to ~89 wt% in vapor phase, were fed in TED in the stages 12 and 2, respectively. The pressure at the tops of TPC, TER and TED were 1, 0.4 and 0.07 atm., respectively. Glycerol/ethanol feed ratio was 1.4.

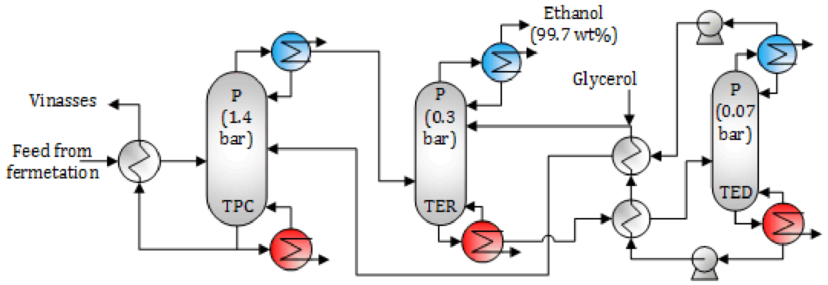


Figure 1-4. Ethanol separation by conventional extractive distillation (C-1)

Ethanol dehydration with VCD had three columns (Fig. 1-5). Vapor from the top of the column TPC was compressed to 3.4 atm. The steam compressed was partially condensed in TPC reboiler. Vapor (89%) from TPC was fed to column bottoms of extractive distillation (TED). Due to high-pressure operation (3.4 atm) in TED, the boiler was eliminated to avoid glycerol decomposition for high temperature operation. The top of extractant regeneration column (TER) was condesed totally and pumped as recycle to TPC. TPC, TED, and TER were designed with 25, 17 and 10 stages, respectively.

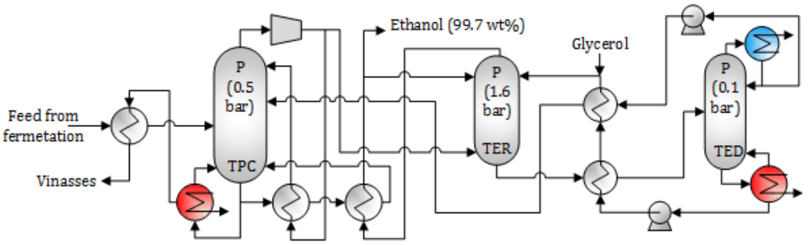


Figure 1-5. Scheme proposed by ethanol dehydration with vapor compression (S-III)

System IV (S- IV) was performed using DED concept. Four distillation columns were used. TPC-LP operates under vacuum (<0.3 atm), while TPC-HP and TED operate at a pressure greater than 1.5 atm. TRE was simulated to 0.07 atm (Fig. 1-6). The condensation heat of TPC-HP and TED were used to supply heat to the reboiler of TPC-LP. The stages number of TPC-LP, TPC-HP, TED, and TER, were 25, 25, 16 and 10, respectively.

1.3. Results and discussion

1.3.1. Isobutanol recovery

S-II with DED allows to reduce the energy requirements of a conventional system from 2 wt% of 10.3 to 5.7 MJ-fuel/Kg-product %; a saving 45% of fuel. The energy requirements for isobutanol separation by S-I was 3.7 MJ-fuel/kg-isobutanol (Table 1), 32% lower than S-II. Heat pump performance was 12.2 (amount of heat energy moved per unit of input work required). Due to the low isobutanol concentration (2 wt %), the highest heat recovery in the distillation processes take place in the preheating with a recuperation of 9.6-11.5 MJ-fuel/kg-isobutanol (Table 1-1).

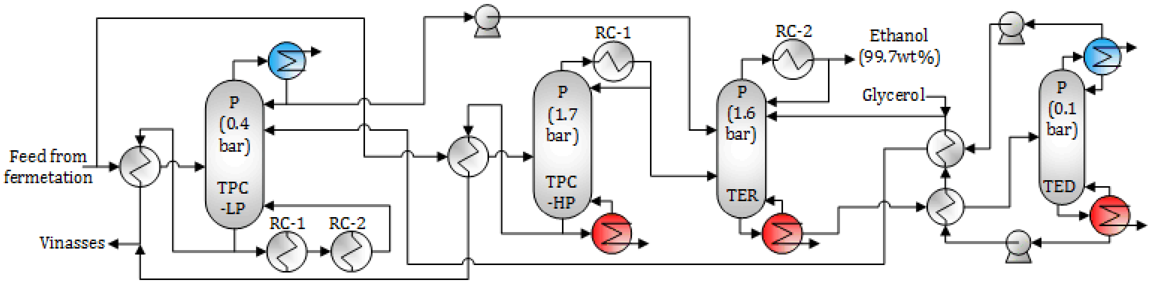


Figure 1-6. Scheme IV (S-IV): double-effect extractive distillation by ethanol dehydration

Vane and Alvarez [39,40] reported that a hybrid process for n-butanol recovery with high selective membrane, vapor compression and distillation required the lowest energy consumption (2.5 MJ-fuel/kg-n-butanol with an minimum approach temperature of 5 ºC). Energy requirement using S-I was reduced to 2.7 MJ-fuel/kg-n-butanol with the minimum approach temperature used by Vane and Alvarez [39,40] (5 ºC). This results suggest that the low energy requirement reported by Vane and Alvarez [39,40] is achieved mainly by vapor compression.

1.3.2. Ethanol recovery

The energy requirement of conventional process with glycerol for dehydration of ethanol from 10 wt% was 5.6 MJ-fuel/kg-ethanol. The boiler heat of TPC, TED and TER were 81.5, 13.5 and 5 wt% of total energy requirement. Energy requirement with the same distillation process using EG as the extractant was 5.8 MJ-fuel/kg-ethanol. Therefore, glycerol did not influence radically the fuel requirement. Fuel consumption with EG for dehydration of ethanol from 12 wt% was 5.2 MJ-fuel/kg-ethanol. Energy requirements for ethanol dehydration from a dilute solution to 12 wt% by a process with dividing wall column are 4.9 MJ-fuel/Kg-ethanol [36] (Table 2). Low energy requirements of these complex structures in ratio with the reported in this work (5.2 MJ-fuel/kg-product) were caused mainly for differences in simulation assumptions.

Table 1-1. Performance for ethanol and isobutanol recovery by heat-integrated distillation

Item	S-II(DED-isobutanol)		S-I(VCD-isobutanol)		SIII-(ethanol-DED)		SIII-(ethanol-VCD)	
	Heat or Work (MJ/kg)	Net fuel (MJ/kg)	Heat or Work (MJ/kg)	Net fuel (MJ/kg)	Heat or Work (MJ/kg)	Net fuel (MJ/kg)	Heat or Work (MJ/kg)	Net fuel (MJ/kg)
Boiler								
C1-LP (C1) or TEP-LP (TEP)	4.3	0.0	7.8	0.0	2.4	0.0	4.3	0.3
C1-HP or TEP-HP	3.4	3.7	-	-	2.0	2.2	-	-
C2 or TED	1.8	2.0	2.0	1.7	0.7	0.8	0.0	0.0
TER	-	-	-	-	0.4	0.5	0.6	0,7
Preheating	9.6	0.0	11.5	0.0	2.2	0.0	2.3	0.0
Compressor	-	-	0.7	2.0	-	-	0.5	1.5
Total	19.0	5.7	21.2	3.7	7.7	3.4	7.8	2.5
Condenser	Heat (MJ/kg)	Net Cold water (MJ/kg)	Heat (MJ/kg)	Net Cold water (MJ/kg)	Heat (MJ/kg)	Net cold water (MJ/kg)	Heat (MJ/kg)	Net cold water (MJ/kg)
C1-LP (C1) or TEP-LP (TEP)	-2,7	-2,7	-6,4	0.0	-1.4	-1.4	-2.6	0.0
C1-HP or TEP-HP	-2,7	0.0	-	-	-1.1	0.0	-	-
C2 or TED	-1,6	0.0	-1,8	0.0	-1.3	0.0	-1.4	0.0
TER	-	-	-	-	-0.5	-0.5	-0.7	-0.7
Total	-7.0	-2.7	-8.2	0.0	-4.3	-1.9	-4.7	-0.7

C1-LP, C1-HP, C2 and C1, C2 were the columns from the Fig.s 2 and 3 for isobutanol recovery, respectively. TEP-LP, TEP-HP, TED, TER and TEP, TED, TER were the columns from the Fig.s 3 and 4 for ethanol recovery, respectively

For comparative purposes, the energy requirements with the same assumptions reported by Ramírez-Márquez et al., 2013 (ideal trays, 86 stages, not pressure drop and fed saturated liquid) were reduced of 5.2 to 4.7 MJ-fuel/kg-product. An energy requirement 0.2 MJ-fuel/kg-ethanol lower than the reported by Ramírez-Márquez et al., 2013. The four main reasons that caused the low energy requirements obtained in this paper in ratio to literature were: fed ethanol to concentration around 89 wt% to the extractive column, the use of a partial condenser in pre-concentration column instead of a total condenser, heat integration and partial recovery of ethanol in extractive column with consequently recycle of ethanol-water from extractant regeneration column.

Table 1-2. Energy requirements of different separation scheme for obtaining anhydrous ethanol

Units	Composition range (wt%)	Total Colum Stages	Energy requirement (MJ-fuel/kg-product)	References
DED	10-93	136	3.6	[107]
Molecular sieves	90-99.3	-	1.4	[93]
Molecular sieves	94-99.8	-	1.3	[100]
Azeotropic distillation	93.5-99.9	54	5.1	[95]
Membrane assisted vapor stripping (Patent)	11.5-99.5	24	2.3	[94]
Extractive distillation (EG-Isooctanol)	12-99.9	-	9.5	[96]
Extractive distillation-dividing wall column (EG)	10-99.8	42	7.4	[111]
Extractive distillation-dividing wall column (EG)	12-99.9	86	4.9	[112]
Extractive distillation-dividing wall column-heat pump (EG)	10-99.7	37	4.5	[110]
Extractive distillation (EG) (Patent)	12-99.6	74	5.8	[100]
Extractive distillation (glycerol)	93-99.3	49	1.1	[99]
Extractive distillation (Ionics liquid [bmim][Oac])	93-99.5	51	3.1	[97]
Extractive distillation (EG and $CaCl_2$)	95-99.8	29	1.5	[98]
Extractive distillation (EG)	12-99.7	52	5.2	This paper
Extractive distillation (glycerol)	10-99.7	52	5.6	This paper
Extractive distillation with DSD (glycerol)	10-99.7	52	2.5	This paper
Extractive distillation with DED (glycerol)	10-99.7	77	3.4	This paper

Energy requirements with S-III and S-IV to obtain anhydrous ethanol (99.7%) from dilute ethanol (10 wt %) were 3.4 and 2.5 MJ-fuel/kg-solvent, respectively (Table 1-1). Energy requirements by S-III and S-IV in ratio to the lowest fuel requirements reported in the literature for a conventional extractive distillation (5.8 MJ-fuel/kg-solvent [23], Table 2) achieved a saving of fuel of 57% and 39%, respectively.

Simulation to obtain hydrous ethanol considering the impurities produced in the fermentation in DED has been studied by Bessa et al., 2012. CO2 is the main impurity because decreases the temperature of condensation. The CO2 impact can be reduced if is separate before to be fed to pre-concentration column or separated at the top of TPC and applying a side stream for vapor phase. For example, CO2 raised the energy requirements of S-III of 3.4 to 3.6 MJ-fuel/Kg-ethanol.

1.4. Energetic evaluation

Due to isobutanol had a higher relative volatility than ethanol (>2 times), isobutanol dehydration was energetically more efficiently than ethanol dehydration to same concentrations (Fig. 1-7). The energy requirements for ethanol and isobutanol dehydration from its respective broth to typical concentrations by VCD were between 2.2 and 3.4, and 3 and 6.7 MJ-fuel/kg-solvent, respectively. VCD for ethanol and butanol recovery decreased the energy requirements of DED between 25 and 30%, and 37 and 48%, respectively. Due to isobutanol has a lower boiling point difference (10 °C) than ethanol dehydration (22 °C) in its respective azeotrope for isobutanol by VCD a higher save was generated.

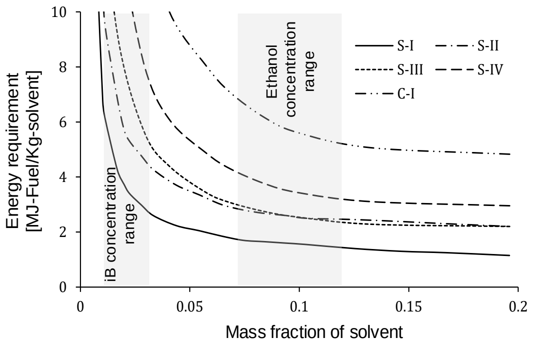


Figure 1-7. The energy requirement achieved for the distillation systems studied in this work. Process S-I and S-II for ethanol dehydration by double-effect distillation and vapor compression. Process S-III, S-IV and C-1 for isobutanol dehydration by double-effect distillation, vapor compression distillation and conventional distillation, respectively.

Fuel requirement was reduced with increase of ethanol concentration of 10 to 20 wt% for S-III, S-IV, and C-I in 0.35, 0.5 and 0.8 MJ-fuel/kg-solvent, respectively. While, an increment in isobutanol concentration of 2 to 20 wt%, reduced the fuel requirement for S-I and S-II in 2.6 and 3.5 MJ-fuel/Kg-solvent, respectively. Confirming the greater potential for butanol than ethanol production in integrated fermentation. However, integrated reactors will be reduce undramatically the energy requirements of isobutanol process (if it declines); because separation units associated with integrated reactors has their own energy requirement (e.g., pervaporation or flash evaporation need compression work due to vacuum, and steam due to evaporation). Noteworthy, the increment in butanol and ethanol concentration beyond 20 wt% reduced slightly the energy requirements.

Separation of ethanol was more favorable than isobutanol from its respective fermentations broth. However, the combustion heat of isobutanol is 26% higher than combustion heat of ethanol (21.1 MJ/L ethanol). On the other hand, the theoretical yield (Rs) for butanol fermentation (41%) is lower than the yield of ethanol fermentation (51%). For this reason, ideal efficiency of separation (IES) process was calculated with next equation:

$$IES = \frac{R_S \cdot (\mathrm{LHV} - H_S)}{LHV_{Glu\cos e}} \tag{1-2}$$

Where, LHV is the lower heating value (MJ-fuel/kg-solvent), and H_S is the energy consumption of separation (MJ-fuel/Kg-solvent), and $LHV_{GLUCOSE}$ is the lower heating value of glucose (16.54 MJ/kg [115]). The differences in IES using DED and VCD for ethanol and isobutanol dehydration were less than 3% (Table 3). Despite similar energy generation per unit of glucose and better properties of isobutanol as biofuel, an economic analysis was necessary for the low concentration of isobutanol produced in the reactor.

1.5. Economic analysis

The TIAC of DED and VCD with an ethanol production of 1.8 ton/h was 1.3 and 1.8 times higher than the conventional distillation process (C-1), respectively. However, TOAC for DED and VCD were 0.55 and 0.41 times lower than C-1, respectively. Consequently, TAC of ethanol dehydration with DED and VCD were 18 and 5 % more economical than C-1, respectively. The high capital annualized costs of VCD were caused principally by compressor investment (Fig. 1-8). Column cost was the item with the lowest effect in TIAC. Meanwhile, heat exchangers (including reboiler and condenser) were the item with higher effect (Fig. 1-8). Due to the effect of TAIC in TAC is reduced with an increasing in biofuel production, when ethanol production was increased ten times, to 18 ton/h, the TAC of DED (S-IV) and VCD (S-III) were 30 and 21% lower than the conventional process (C-I), respectively.

Table 1-3. Energy generation with separation schemes evaluated in this work for the purification of isobutanol and ethanol

System	Solvent	Theoretical yield [g biofuel/ g glucose]	Separation Heat [MJ-fuel/Kg-solvent]	LHV° [MJ-fuel/kg-biofuel]	Ideal efficiency of separation
S-I	Isobutanol (2 wt%)	0.41	3.7	34.4	0,77
S-II	Isobutanol (2 wt%)	0.41	5.7	34.4	0,72
S-III	Ethanol (10 wt%)	0.51	2.5	27	0,76
S-IV	Ethanol (10 wt%)	0.51	3.4	27	0,73

°116

TAC of isobutanol dehydration with DED (S-II) and VCD (C-1) for isobutanol production of 1.8 ton/h were 24.5 and 12 % less expensive than the conventional process (Fig. 1-8). Due to the smaller boiling point difference, VCD for isobutanol recovery was more efficiently than VCD for ethanol dehydration. Due to the higher ethanol concentration from fermentation broth, TOAC and TIAC for ethanol separation were between 25 and 47%, and 44 and 58 lower than isobutanol dehydration, respectively. TAC of ethanol separation was 43-47% lower than isobutanol dehydration with its respective technologies (Fig. 1-8).

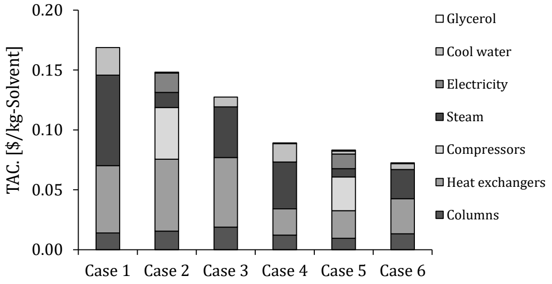


Figure 1-8.. Economic evaluation. Solvent flow production: 1800 kg-product/h. The ethanol concentration of cases 4, 5 and 6 was 10 wt%. The isobutanol concentration of cases 1, 2 and 3 was 2 wt%. The case 2 and 5 used vapor compression distillation. The case 3 and 6 used Double-effect distillation. The case 1 and 4 was the conventional distillation.

1.6. Conclusions

The energy requirement of ethanol dehydration by the conventional distillation process, studied in this work, was reduced by DED and VCD in 39-40 and 54-57%, respectively. Due to the higher net heating value of isobutanol, the energy efficiency of isobutanol and ethanol recovery was approximately equivalent. TAC of isobutanol separation was 40-47% higher than ethanol fermentation due to low butanol concentration from fermentation. When the butanol or ethanol concentration are increased to 20 wt% by an integrated reactor, the energy requirement of separation unit in hybrid fermenters must be lower than 0.5 and 3.5 MJ-fuel/kg-product for ethanol and isobutanol production, respectively, to decrease the energy requirements of DED.

2. Evaluation of alternative separation processes for acetone, butanol, and ethanol (ABE) recovery by heat-Integrated distillation

Abstract

Four processes of heat-integrated distillation were proposed and evaluated for acetone, butanol, and ethanol (ABE) recovery. The distillation-intensified systems were simulated in Aspen Plus® software. Double effect system with four columns was the most economical process (0.12-0.16 $/kg-ABE). Double-effect process for recovery from Chinese industrial and Clostridium acetobutylicum JB200 titers achieved energetic requirements of 8.7 and 6.1 MJ-fuel/kg-ABE, respectively. Process with vapor compression distillation (VCD) reached the lowest energy requirements (between 4.7 and 7.3 MJ-fuel/kg-ABE). Due to the high investment cost of compressors, VCD was more expensive than double-effect process. Energy requirement of the distillation systems studied in this work were among the lower energy requirements reported in the literature by ABE recovery. Therefore, the results achieved in this work provide a baseline for decrease to alternative separation technologies.

Keywords: *Heat pump, double-effect, and integration*

Paper under review

2.1. Introduction

N-Butanol is a solvent and chemical with a global demand in 2009 of six billion dollars [1]. Butanol cost is strongly tied to oil because it is obtained mainly by petrochemical route [2]. During the last years, its biotechnological production has been renewed by biofuel potential [2,3]. The developing and economic expansion of China during the last years is one example of this, where annual butanol production was 2.1x105 tons in 2008 and is expected to reach 1x106 tons in the next few years [3].

The biotechnological production is traditionally performed by mesophilic solvent-producing strains [4], such as Clostridium acetobutylicum, Clostridium beijerinckii, Clostridium saccharobutylicum or Clostridium saccharoperbutylicum. In Chinese industrial process, acetone, butanol, and ethanol (ABE) are produced in the average ratio of 2.5:4.8:1 (calculated from stoichiometric reaction reported by Ni and Sun [3]). In 1994, the total production of acetone was 3.8x106 tons [5]. Ethanol is the primary additive of gasoline. The main advantage of traditional Clostridium is the ability to consume a wide variety of substrates, such as glucose, sucrose, lactose, xylose, starch and glycerol [6,7].

Low substrate concentration (55-75 g/L), to achieve a high conversion, are fed into the reactor for product inhibition. This characteristic makes steam consuming operations, such as mash sterilization, downstream product recovery and wastewater treatment- highly energy demanding[8]. Utilities in a butanol plant based on corn is approximately three times higher than ethanol production [9]. In Chinese industrial processes has been reported a great steam consumption 13-25 kg-steam/kg-ABE [3]. However, Jilin Cathy Industrial Biotech reported a low energy requirement of distillation system of 6-7 kg-steam/kg-butanol [10].

Integrated reactors with separation units have been proposed to reduce energetic requirements, investment cost and vinasses production [11–15]. Due to selective separation, the butanol toxicity and the product inhibition in integrated reactors is reduced. Qureshi et al. [11] reported that liquid-liquid extraction and adsorption processes have the lowest energy requirements with 8.9 and 8.2 MJ/kg-butanol, respectively. Kraemer et al. [16] developed an integrated reactor with external extraction using mesitylene as the extractant. Energy consumption of this system is of 4.8 MJ/Kg-butanol. Dual novel extraction has been proposed to reduce the toxicity of an extractant with high butanol distribution coefficient [17]. Mesitylene is used as a nontoxic solvent to remove the toxic extractant before to be fed to the reactor. Total energy requirement of recovery achieved with n-decanol and mesitylene was 3.8 MJ/kg-butanol. However, low concentration of product was achieved (Purity of butanol, acetone and ethanol were 0.95, 0.9, and 0.2, respectively).

Final purification of integrated and conventional reactors is traditionally carried out by distillation. Process integration in distillation follows various routes such as: internal heat integrated distillation columns [18,19], vapor compression distillation (VCD) [20,21], petlyuk or dividing wall columns [22–25], double-effect distillation (DED) [26,27] and cyclic distillation [28–30]. Among these alternatives, Kaufman et al. [20] proposes a sequential system of multiple VCD by ABE recovery. Sanchez-Ramirez et al. [31] optimized several configurations without condensation heat recovery (DED or VCD) by ABE purification. In this work, four heat integrated distillation systems were proposed and studied energetically and economically. Distillation configurations will provide a baseline for comparison to other separation processes.

2.2. Process model

The simulations were performed in Aspen Plus®. RadFrac was the unity used for distillation simulation. The base method in simulations was UNIQUAC-RK with CO2 and H2 as Henry's components. Due to greater precision to low pressure and concentrations of vapor-liquid equilibrium (VLE) [32], parameters for butanol-water mixture were the reported by Fisher and Gmehling [33]. The binary parameters of the decanter unities was APV73 LLE-ASPEN due to the low accuracy of UNIQUAC, or NRTL parameters, in ratio to experimental liquid-liquid equilibrium data [34,35] (Fig. 2-1).

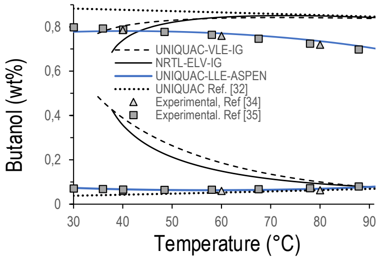
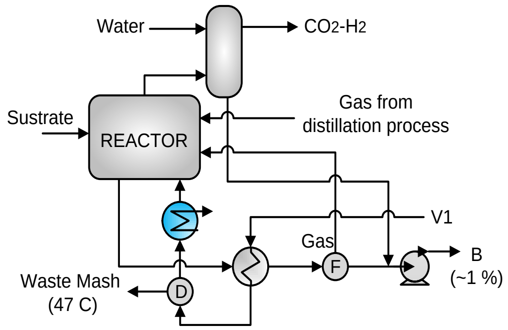


Figure 2-1. Liquid-liquid equilibria (LLE) of butanol/water system to several temperatures. Experimental data [117,118].

Energetic evaluations were performed in fuel equivalent. Vapor and electricity efficiencies were assumed as 0.9 and 0.33, respectively [36]. Energetic integration was performed with 10 ºC of approach temperature. Compressor efficiency was 0.75. Columns were simulated with Murphree efficiency of 0.6. Trays selection was sieve's type. Pressure drop in column was calculated with tray rating of RadFrac. Glucose and solids (cellulose) were fed at 160 and 40 gL-1, respectively. Glucose conversion in the reactor was 0.83. The production capacity of solvents was 5000 kg-ABE/h for each simulation. Configurations were studied chiefly based on ratio of Chinese industrial process. Additionally, ABE recovery from downstream of three hyper-butanol mutant strain were studied. In all simulations, the purity of butanol, acetone, and ethanol achieved were 0.997, 0.99 and 0.89, respectively.

Vinasses were obtained in the bottom of the first column for all configurations. Vinasses were recirculated into the reactor for sugar dilution (Fig. 2-2) due to stillage is recycled in ~40% to reduce substrate concentration in Chinese industry[3]. Non-condensable products were compressed and recycled to the stripping column (10 stages). Cold water (10000 kg/h) was used for solvent recovery of non-condensable stream. Vinasses obtained in all configurations were used to preheat the distillation fed (Fig. 2-2).



(a) Direct bleeding

Figure 2-2. Fermenter with stillage recycle

The total annualized cost (TAC) was calculated from:

$$T.AC = \frac{TOAC + {TIAC}/{t_{ri}}}{F_{ABE} \cdot t_a} \qquad (1)$$

Where F_{ABE} is the production flow (kg-ABE/h), $t_{ri,}$ is the payback period (3 years), t_a, annual operation time (8150 h), TOAC ($) is the total operational annualized cost and TIAC ($) is the total investment annualized cost. Equipment cost was calculated with functions reported by Douglas [114]. Costs of steam, cooling water and electricity and Marshall & Swift equipment cost index (M&S) were assumed as 16 $/kg, 0.006 $/kg and 0.126 $/kWh and 1625, respectively. Process equipment was designed using stainless steel material. Energy requirement was calculated with an efficiency in the production of steam and electricity from fuel of 0.9 and 0.3, respectively.

2.2.1. Description of distillation systems with heat integration

Vinasses were obtained in the bottom of the first column for all configurations. Butanol boiling point is bigger than water; however, the azeotrope of minimum point boiling with water increased volatile relative of butanol. Indeed, butanol has a relative volatility at low concentrations in water 2.3 times higher than ethanol. Azeotrope can be break using the low solubility of butanol with a decanter. In all configurations, the aqueous phase was recycled to a waste mash column. A decanter was used after each stage of separation in the scheme thermally integrated with 4 distillation columns (4DC), in order to decrease the concentration of water in the feed of each column. Temperature decanting was fixed at 40 ºC. ABE was sequentially separated in terms of its boiling point (Figure 2-2).

Butanol boiling point is higher than water. However, the azeotrope of minimum point boiling with water increased the volatile relative of butanol. Indeed, butanol has a relative volatility at low concentrations in water 2.3 times higher than ethanol. For this reason, butanol in all processes is recovered from vinasses in the top of column C1.

ABE in the process with four distillation columns (4DC) was sequentially separated in terms of its boiling point (Fig. 3). ABE to concentrations of ~40 wt% was obtained in the top of C1. Reflux in C1 was not used due to butanol-water azeotrope. The concentration of water was reduced with decanters (Fig. 3). Temperature of decanters was fixed at 40 ºC (see Fig. 1). Binary azeotrope of butanol-water was break with a decanter. In all configurations, the aqueous phases after decantation were recycled to column C1.

Acetone, ethanol, and butanol were obtained in columns C2, C3 and C4, respectively. The total stage numbers of all columns and process can be found in Table 1. Low-pressure columns were proposed to use the heat of condensation of column C1. Exchanger condensation area for low-pressure columns and columns diameter can be increasing by low operation temperature. However, this effect is not necessary true in the acetone column (C2), due to increase of acetone volatility at low pressures [119–121] (Fig. 4).

Total stage in the configuration with 3 distillation columns (3DC) were reduced of 90 at 70 (Table 1). In the first column (C1), acetone and ethanol were obtained mainly in the top stage. Side stream to decanter in C1 was used for breaking butanol-water azeotrope. Organic phase was fed to butanol column (C3) and aqueous phase was recycle to C1. Similar than 4DC, low-pressure columns were proposed to end ABE purification (Fig. 5). Heat integration is difficult because condensation temperature in the top stage of C1 was relatively low (62 ºC) because butanol was not present. Therefore, intermediate condensation in C1 (stage 15) was used to apply its heat in C2 and C3 boilers. Acetone and ethanol were purified simultaneously in C2. Butanol was purified in C3.

The vapor compression process had three distillation columns (3DC-VC), see Fig. 6. The configuration of streams in 3DC-VC was different to 3DC. In C1, one side stream was not used to increase the temperature of condensation. The vapor on top of column C1 was split into two streams. One stream was compressed and another was not. It reduced the compression work. The condensation heat of compressed stream was applied in boiler of column C1. The condenser heat of vapor not compressed was used in boilers of low-pressure columns (C2 and C3). In the columns C2 and C3 vapor compression was not considered due to the high temperature difference between its condenser and boiler (42-45 ºC). Acetone was obtained from the top of column C2. Ethanol on the top and butanol on the bottoms of column C3 were obtained. The fuel consumption of this configuration was given by the steam requirement of C1 and the compressor work.

The double effect process had four distillation columns (4DC-VC). Stream after fermentation was divided in two streams, preheated and fed to columns C1 and C1-LP (Fig. 7). In this system, columns C1 and C3 operated at a pressure moderately higher than atmospheric pressure to improve the heat integration. The heat of a side condenser in column C1 was used to apply its condensation heat to boiler of low pressure columns. C1-LP and C2 in the top stage had a pressure of 0.3 and 0.5, respectively. Split ratio of stream after fermentation was iterated until the sum between condensation heat of C1 and C3 and boiler heat of C1-LP and C2 become null. The total energy consumption of 4DC was given by the steam requirement of columns C1 and C2.

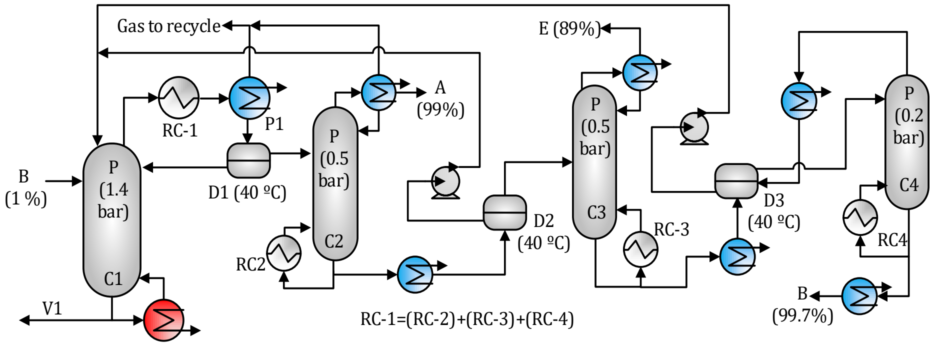


Figure 2-3. Heat-integrated configuration with 4 distillation columns (4DC) proposed by ABE recovery

Acetone, ethanol, and butanol were obtained in columns 2, 3 and 4 respectively. Stage numbers in C1, C2, C3 and C4 columns were 20, 30, 30 and 10 respectively. Low-pressure columns were proposed to use the heat of condensation of column C1. This increases exchanger condensation area for low-pressure columns. However, in acetone column low pressure was advantageous because acetone volatility increased at low pressures [119–121] (Figure 2-3).

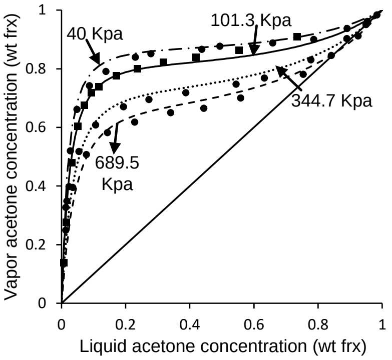


Figure 2-4. Vapor-liquid equilibria (VLE) of acetone/water system to several pressure. Continues lines: UNICUAC prediction (APV73 VLE-LIT Aspen Plus ®). Points: experimental data [119–121].

In the configuration with 3 distillation columns (3DC), total stage were reduced to 80 at 65 avoiding unnecessary condensations. In the first column (C1), acetone and ethanol were obtained mainly in the top stage. Similar than 4DC, low-pressure columns were proposed to ABE recovery (Figure 2-4). In C2 column, acetone and ethanol were produced simultaneously. Condensation temperature in the top stage of C1 was relatively low (62 ºC) because butanol was not present. An additional intermediate condensation was used to reduce exchanger area of condensation and increasing energetic integration. Intermediate condensation in C1 (15 stage) was used to apply its heat in C2 and C3 boilers. Lateral stream to decanter in C1 was used for breaking butanol-water azeotrope.

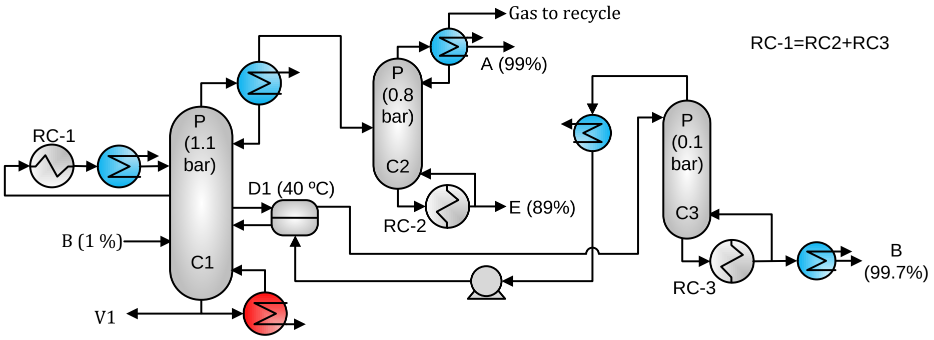


Figure 2-5. Scheme with 3 distillation columns (3DC)

Vapor compression configuration had 3 distillation columns (3DC-VC). In this configuration, the vapor of C1 was compressed only. Not all vapor of C1 was compressed because a part was used to apply heat into low-pressure columns (C2 and C3). Vapor compressed was used to apply heat condensation in C1 boiler. In C2 and C3 vapor compression was not considered due to the high difference of boiling point (42-45 ºC). In C2 column acetone was obtained in the top stage. Butanol and ethanol were produced simultaneously in C3 column (Figure 2-5).

Double effect configuration had 4 distillation columns (4DC-VC). Stream after fermentation was divided, preheated and fed to C1 and C2 (Figure 2-6). In this scheme, C4 and C1 operated at a pressure moderately higher than atmos. pressure. C2 and C3 in the top stage had a pressure of 0.3 and 0.5 respectively. Lateral condensation in C1 was used to apply its condensation heat to the low-pressure boiler. The total energy demand of this configuration were given by C1 and C2 steam requirement.

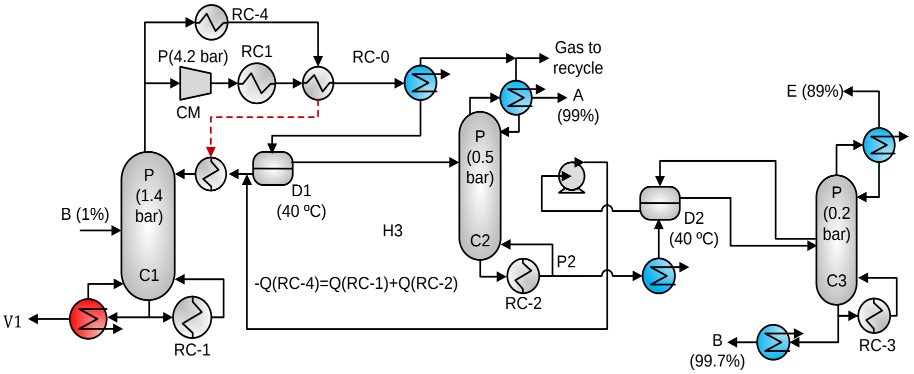


Figure 2-6. Configuration with 3 distillation columns and vapor compression (3DC-VC)

2.3. Results and discussion

4DC and 3DC configuration without heat integration and Chinese industrial yield achieved 32.1 and 30.1 MJ-fuel/Kg-ABE respectively. Heat integration allows that 4DC and 3DC configurations were equivalents (~11.5 MJ-fuel/kg-ABE, Table 1). Biggest energy integration was obtained in preheated (16.6 MJ-fuel/Kg-ABE) due to low solvent concentration (20 g-ABE/L). Butanol recovery target was not sufficient for total ethanol recovery in C1, therefore with vinasses recycle ethanol recovery was improved. Ethanol recovery was more difficult than butanol recovery because the concentration and relative volatility of ethanol were lower than butanol. Energy requirement without vinasses recycle was 18.8% bigger for achieving the same ethanol recovery of 4DC.

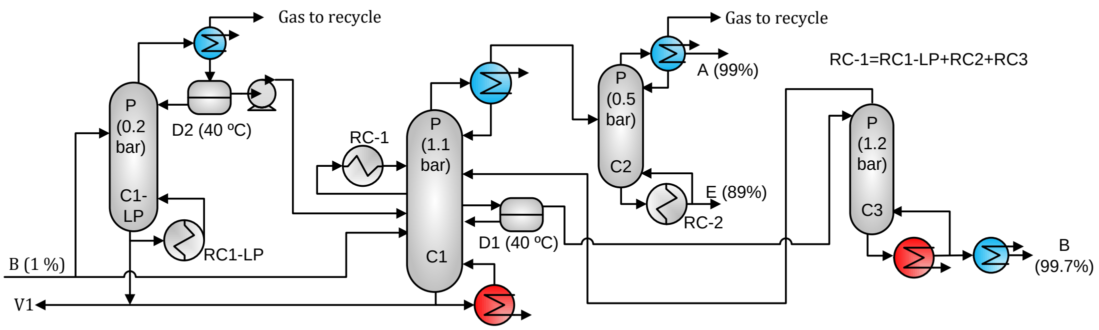


Figure 2-7. Configuration with 4 distillation columns and double effect integration (4DC-DE)

Total energy requirement without integration for ethanol, acetone and butanol purification columns (C2, C3 and C4, respectively) with 4DC was 3.2 MJ/kg-ABE; while with 3CD configuration was 1.7 times lower due at less unnecessary condensation. With industrial Chinese yield, TAC of 3DC was only 3.8 % lower than 4DC due to heat integration and low product concentration of fermentation. In 4DC and 3DC configurations, the operational cost was equivalent at approximately 58% of TAC. Exchanger cost was the 78% of total investment.

3DC-VC configuration reduces energetic requirement in comparison with 3DC in 37 %. Consequently, TAOC decreases in 33%. However, the high cost of compressors increases the investment for 31%. Therefore, the total economical requirement of separation with 3DC were equivalents to 3DC-VC. Coefficient of performance (COP) of pump heat was 8.4. 3DC-VC had energy requirement of 7.3 MJ-fuel/kg-ABE.

In the literature lowest energetic requirement was achieved with membrane assisted vapor stripping (MAVS) (4.2-MJ-fuel/Kg-ABE (3/6/1) at 2 wt% of ABE[116,122]). In this configurations, pressure drop and CO_2 effect was not considerate and 5ºC approach temperature, ideal stage and 90% ethanol recovery were supposed. Using 5ºC approach temperature between the bottom and feed streams to the first column with 3DC-VC, energetic requirement are reduced of 7.3 at 6.4 MJ-fuel/Kg-product. Using a ratio of ABE of 3/6/1, 5ºC approach temperature and 90% ethanol recovery by ABE recovery from 2 wt%; energetic requirement was reduced to 5.8 MJ-fuel/kg-product mainly.

In integrated configurations with condensation heat recovery it is important to including pressure drop and CO_2 impurity in simulation calculation. CO_2 impurity decreased condensation temperature increasing exchanger area of hybrid boiler-condenser or compressor work. CO_2 is the most important impurity in ethanol recovery by double-effect distillation [107]. For this reason, when CO_2 and H_2 were depreciated energy requirement were reduced of 5.8 to 4.9 MJ-fuel/kg-ABE. Assuming ideal gas and null pressure drop energy consumption was reduced from 4.9 to 4.5 MJ-fuel/kg-ABE. This energetic requirement was only 7% bigger than MAVS. However, it is important to mention that non-condensable, pressure drop, among others, can have a different effect in MAVS and non-recycle of vinasses are realized in MAVS.

4DC-DE allow to decreasing energetic requirements of conventional distillation with low capital investment (Table 2-1). The investment was increased for the extra column and less temperature difference between the low-pressure column and intermediate condensation heat of high-pressure column (C1). Dehydration butanol column was not operated with a vacuum pressure. 4DC-DE had an operational cost 21% higher than 3DC-VC. However, 4DC-DE is the most economical option because had an investment cost 31% lower than 3DC-VC.

Less energy requirement and TAC were obtained using hyper-butanol producing *C. acetobutylicum JB200.* Using *C. acetobutylicum JB200, C. beijirinkii BA101* and *C. acetobutylicum SolRH,* energetic cost and TAC of *4DC-DE* were reduced in 30, 26 and 27%, and 25, 22, and 22% respectively. This reduction was caused for less sub-product yield and bigger butanol concentration achieved in the fermentation. Mariano et al. reported energetic requirement for ABE recovery using *C. beijirinkii BA101* was 15.2 MJ-fuel/kg-ABE; using 4DC-DE energetic requirement were reduced in 59% in ratio to Mariano et al.[123] reported.

Several energetic analysis of integrated reactors has been reported in the literature[66,89,124]. The most attractive energetically recovery units reported by Qureshi et al.[89] were adsorption, liquid extraction, and pervaporation. Energy consumption of pervaporation reported by Groot et al.[66] and Qureshi et al.[89] are 9 MJ/kg-ABE and 14 MJ/kg-butanol or 10.9 MJ/kg-ABE10.9 MJ/kg-ABE (calculate in this work from *C. beijirinkii BA101 ratio*) respectively. Energy requirement of liquid extraction and adsorption reported by Qureshi et al.[89] for *C. beijirinkii BA101* are 8.9 and 8.2 MJ/kg-butanol or 7.1 and 7.7 MJ-fuel/Kg-ABE (calculated in this work assuming steam efficiency of 0.9) respectively.

Energetic consumption of 4DC-DE and 3DC-VC were 29.1 and 34.8% and 17.9 and 10.7 % lower than reported by Qureshi et al.[89], for liquid-liquid extraction and adsorption respectively. However, the integrated reactor can better the fermentation productivity. Integrated reactor needed final purification because are not 100% selective; for this reason can be coupled with configurations of thermally integrated distillation studied in this work and reduce its total energetic requirements.

Table 2-1. T.A.C. and energy recovery of different heat integrated distillation configurations[b]

Biocatalyst	Butanol titer $[gL^{-1}]$	Solvent ratio: A/B/E	Scheme	ABE recovery	Fuel requirement [MJ/Kg-ABE]	TAIC [$/Kg-ABE]	TAOC [$/Kg-ABE]	T.A.C. [$/Kg-ABE]
Typical microorganisms in Chinese industrial process	10	2.5/4.8/1	4DC	0.970	11.7	0.084	0.113	0.197
			3DC	0.969	11.5	0.078	0.111	0.189
			3DC-VC	0.970	7.3	0.115	0.075	0.190
			4DC-DE	0.969	8.7	0.079	0.080	0.159
C. Beijirinkii BA101 [123]	19.7	6/24.6/1	3DC	0.976	7.6	0.064	0.074	0.138
			3DC-VC	0.977	5.0	0.088	0.052	0.140
			4DC-DE	0.980	6.3	0.064	0.059	0.123
			5DC [a]	-	15.2	-	-	-
C. acetobutylicum SolRH [125]	18.5	4/8.4/1	3DC	0.977	7.8	0.062	0.076	0.138
			3DC-VC	0.981	5.0	0.087	0.053	0.140
			4DC-DE	0.977	6.5	0.063	0.061	0.124
			5DC [a]	-	12.6	-	-	-
C. acetobutylicum JB200 [126]	20.4	5/9.2/1	3DC	0.977	7.0	0.059	0.069	0.128
			3DC-VC	0.976	4.7	0.083	0.050	0.133
			4DC-DE	0.978	6.1	0.062	0.057	0.119

[a] Calculated from reference [127] . [b] Ethanol dehydration costs and energy recovery for anhydrous ethanol production were not included

2.4. Conclusions

Distillation is considered conventionally an inefficient alternative by ABE recovery; however, with the configurations investigated in this paper, distillation was an alternative energetically attractive. Using double-effect and vapor compression distillation, energetic requirement were between 4.7 and 7.3 MJ-fuel/kg-ABE and 6.1 and 8.7 MJ-fuel/kg-product respectively. Heat integration distillation can compete energetically with the integrated reactor, but is necessary determine the economic benefits of integrated reactors with respect to non-hybrid reactors. The most economical option was double effect distillation with recovery cost between 0.12 and 0.16 $/kg-product.

3. Extractant regeneration with direct steam distillation in acetone, butanol, ethanol (ABE) extractive fermentation

Abstract

Extractant regeneration and acetone, butanol and ethanol (ABE) purification were studied in this work for ABE production with extractive fermentation. Regeneration of high-boiling extractants, usually biocompatibles, required high preheating, high-pressure steam and vacuum operation. In this work was proposed and evaluated economically and energetically direct steam distillation (DSD) for extractant regeneration. The simulations were performed by Aspen Plus® software. DSD column was operated to atmospheric pressure with low-pressure steam and low preheating energy. Oleyl alcohol and oleyl alcohol-decanol (80/20 w/w) mixture were feeding in DSD configurations. Comparison with conventional regeneration, dual extraction and high-temperature extraction to equivalent conditions was realized. Heat integration was applied to reducing the heat of ABE purification by distillation. DSD was the scheme with lowest energy requirement and TAC.

Keywords: heat integration, hybrid reactor, biobutanol; mixture extraction

Paper under review

3.1. Introduction

Acetone, butanol and ethanol (ABE) production by biotechnological route was the second fermentation in importance in the world of middle XX century [4]. However, was unable to compete with the petrochemical production. Actually, interest in biobutanol production by fermentation is increasing because butanol and ABE mixed are considered an alternative biofuel [128]. Butanol and acetone have 27 and 9.6% more energy content than ethanol, respectively [116]. ABE production is not viable economically with conventional technologies. In perspective, ABE process has productivities, concentration product, and yield fermentation 2-3, 4-5 and 1.5-1.7 times lower than ethanol conventional production, respectively. ABE fermentation is carried out by several strains of solventogenetic Clostridium, such as *Clostridium acetobutylicum* [129]. Butanol is the main inhibitor in ABE fermentation and caused inhibition total at concentrations between 13 and 19 gL^{-1}.

The integrated reactor has been proposed to reduce butanol inhibition. In this process, butanol is selectively separated from the reactor. Therefore, sugar concentration and performance of fermentation can be increasing. In the literature, integrated reactor with evaporation flash [88], pervaporation [55], adsorption [89], gas stripping [126], pertraction [63] and extraction liquid-liquid [130] has been proposed. Extractive fermentation is one of the recovery options with lower energetic requirements reported in the literature [66,67,89].

Solvent selection is complex because several requirements are necessary for the extractant [131], such as biocompatibility, non-emulsion forming, easy regeneration, high selectivity, low viscosity, high butanol distribution coefficient, availability, and cost. Additionally, several configurations have been proposed by extractive fermentation. Low energy fermentation with dual extraction (DEx) [132] and high-temperature extraction (HTE) [131] has been proposed by ABE production. An example of high-temperature extraction, using mesitylene as extractant, is the configuration proposed by Kraemer et al. [131].

HTE is used to increasing butanol distribution partition, therefore less extractant is needed. Mesitylene has a mass partition coefficient of butanol of 0.86 at 30 ºC and 3 at 80 ºC [131]. High selectivity (1970) and medium boiling temperature (180 ºC) are the mains advantage of mesitylene. Kraemer et al. [131] suggest that mesitylene is a nontoxic extractant by its low solubility in water. However, experimental toxicity in biocatalyst is still unknown.

DEx was proposed for use toxic solvents with high butanol distribution coefficient. The extractant toxic is removed with a biocompatible solvent before to recirculate aqueous phase to the reactor. This configuration cannot improve the fermentation productivity, due direct contact of biocatalyst with the toxic extractant. However, allow using high substrate concentration. Therefore, waste water and energy requirement of downstream and treatment are reduced significantly. DEx has been used with high butanol distribution extractant (decanol (DAL) (7.1) or octanol (10)) and mesitylene as the biocompatible extractant. DAL was the most promising extractant [132].

Biocompatibility is a more advantageous characteristic of extractant because is used directly in fermentation and butanol productivity of fermentation can be increased. Oley alcohol (OAL) has been the most studied extractant, to carry out in situ extractive fermentation because has acceptable butanol distribution coefficient (3.5-4.5) and high selectivity (>300) [133]. However, high boiling temperature (360ºC) of OAL make difficult extractant regeneration because are needed high preheated, low-pressure distillation, and high-pressure steam. The combination of toxic solvents and non-toxic OAL has been proposed to decrease boiling temperature and increasing butanol distribution coefficient [133,134]. The mixing ratio is limited by the biocompatibility of toxic extractant. DAL has been frequently proposed in mixed with OAL in ratio 80/20 OAL/DAL. However, non-toxic ratios as large as 60/40 has been reported [133].

An alternative method for extractant regeneration was proposed in this work. The method proposed, direct steam distillation (DSD), in this work can to operate at atmospheric pressure using low-pressure steam. Atmospheric pressure operation increasing energetic integration, because condensation heat can be used in a reboiler at low pressure; and decreasing the preheating size. In this work, high-temperature extraction; dual extraction; OAL and mixed extraction using conventional low pressure system and DSD for extractant regeneration were compared energetically and economically.

3.2. Process model

ABE extractive fermentation was simulated in Aspen Plus ®. Equilibrium liquid-vapor, extraction column and decanter in distillation columns were simulating with UNIQUAK-RK, UNIFAC-LL and NTRL, respectively. Butanol-water parameters of UNIQUAC-RK was proposed Fisher and Gmehling [135]. APV73 LLE-ASPEN was the parameters set of butanol-water fixed in NTRL. Missing parameters were estimated from UNIFAC. CO_2 and H_2 were simulated as Henry components. Extraction liquid-liquid was realized in 5 stages. Butanol extraction efficiency was fixed to 0.8. Water recycle into the reactor was fixed to 0.75. Solvent flow in each simulation was found to keep butanol concentration into the reactor in 10 gL^{-1}.

In this paper was used a stoichiometric ratio of A/B/E industrial production in China (4.8/2.5/1) [136]. Total glucose conversion was fixed in 0.8. Substrate concentration was selected as 200 gL^{-1}. ABE end recovery was 0.97. Ethanol, butanol and acetone purity were 99, 99.5 and 89 wt%, respectively. Murphree efficiency in tower distillations was 0.7. Distillation columns were simulated with sieve trays and pressure drop was calculated with tray rating. Efficiency in steam production in ratio to fuel was fixed in 0.9. Heat exchangers were performed with 10º C approach temperature.

The scheme proposed in this work for ABE purification had 3 distillation columns (Figure 3-1). Vinasses and acetone purification were realized in the AC and WC columns, respectively. AC and WC were operating to pressure in the top of 0.27 and 0.45, respectively. In EBC column, butanol and ethanol were purified to 1.7 bar. In this way, heat condensation of EBC can be used to provide heat to AC or WC boiler. The stage number of WC, AC and EBC columns were 20, 30 and 30, respectively.

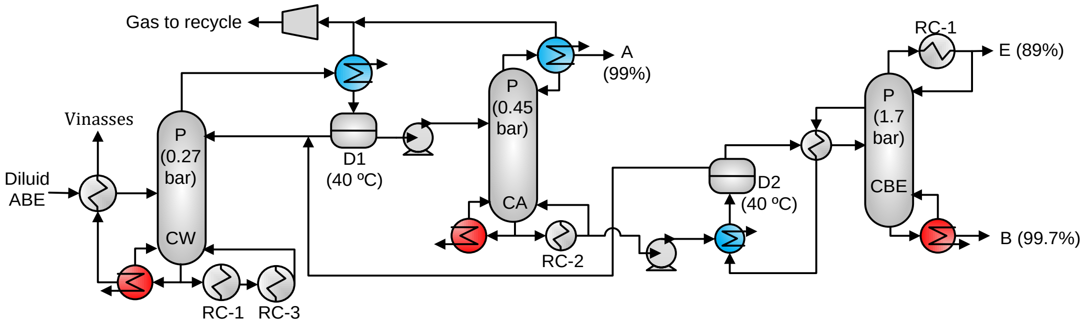


Figure 3-1. End recovery scheme proposed in this work to ABE purification

In external dual extraction, the toxic solvent was decanol and the biocompatible solvent was OAL. Mesitylene was used in high-temperature extractive fermentation. Mesitylene was simulated with butanol, acetone, ethanol, and water distribution coefficient constant of 2.2, 0.83 and 0.1 [131] respectively. Mesitylene toxicity is unknown, however in this work will be considered biocompatible as proposed Kraemer et al. [131].

Marshall & Swift equipment cost index (M&S) was 1536.5 [137]. Equipment was simulated using stainless steel materials. Installation cost of each extraction stage was performed as pressure vessel with height/diameter ratio of 3; and total residence time (aqueous and organic phase) of 0.5 h, because was found, experimentally, the contact time necessary for an efficient extraction [134]. Stage extraction cost was not calculated for biocompatible extractants because these increasing reactor productivity in ratio to conventional fermentation. Extractants and parameters cost used in economic evaluation can be observed in the Table 3-1 [138,139].

3.3. Results and discussion

3.3.1. High temperature extraction

In integrated reactors, substrates at higher concentrations than the conventional can be fed (>60 g/L). In the configuration proposed by Kraemer et al. [131] bleeding is not required because is used a substrate concentration as high as the extractant selectivity. However, from practical viewpoint bleeding is necessary because fed concentration substrate must be limited for the presence of solids (e.g. lignin, cellulose, hemicellulose, salts, ash) and possible toxic compounds (e.g. furans, organic acids or phenolic compounds); and available substrate concentration.

Tabla 3-1. Parameters used in economic evaluation

Unity	Valor	Unity
Low-pressure steam (3 bar)	2.2	\$/ton[139]
Mid-pressure steam (30 bar)	7.9	\$/ton [139]
High-pressure steam (105 bar)	11.8	\$/ton[139]
Oleyl alcohol	4.3	\$/kg [138]
DAL	2.1	\$/kg [138]
Mesitylene	2.9	\$/kg [138]
Cool water	0.06	\$/ton
Electricity	0.095	\$/kWh
Operation time (t_o)	8150	H
Production flow	5000	kg-ABE/h
Time of return investment (t_{ri})	5	Year

Additional assumptions proposed by Kraemer et al. [131] are: ABE instead of glucose is feed into “reactor” implying a glucose conversion of 100%; non-condensable is not feed to reactor; extraction stage number is 21; and final ethanol concentration is 14 wt%. With these assumptions is reported low energy requirements by ABE recovery, 4.8 MJ/Kg-butanol or 3.3 MJ-fuel/Kg-ABE (calculated in this work assuming 90 and 33% efficiency in steam and electricity production and A/B/E ratio of 3/6/1).

In external extraction if nontoxic extractant is used there are two bleeding options (see Figure 3-2). In recirculation option 1, bleeding is direct from the reactor while in option 2 is after the extraction. Therefore, in recirculation option 2 more extractant is necessary and is achieved a bleeding stream with less butanol composition. The feasibility of these options depend on the amount of extractant used, and the decreased energetic requirements in WC column. HTE with direct bleeding needs 75% less extractant than recirculation option 2 to keep 1 wt% butanol concentration in the reactor. In option 2, mesitylene/ABE ratio used in the simulation was 24/1.

Bleeding direct from the reactor was the best option because mesitylene has a poor ethanol distribution coefficient (0.1). Energetic requirements of WC depended mainly on ethanol recovery because ethanol has relative volatility 2.5 times less than butanol. Energetic requirement obtained in this work were 2.5 times bigger than reported by Kraemer et al. [131]. Low energy efficiency obtained in this work was caused mainly by low substrate concentration feed to the reactor and different assumptions. Total installation cost was \$13.4MM. TAC of high-temperature extraction with direct bleeding was 0.097 \$/kg-ABE. Investment costs of heat exchangers and steam requirement (0.047 and 0.02 \$/kg-ABE, respectively) were the items more important in economic evaluation.

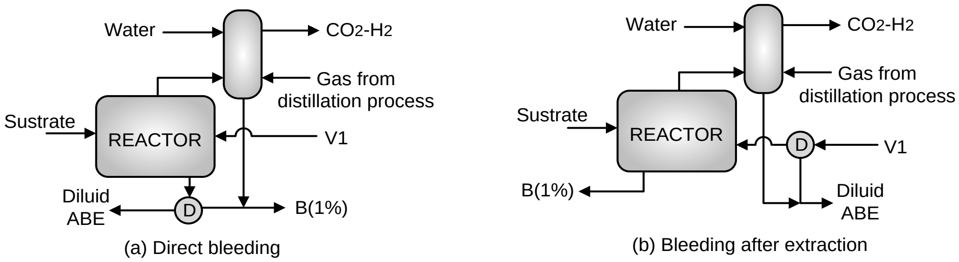


Figure 3-2. Alternatives of bleeding in external extractive fermentation

Without integration, preheated before extraction was 50% of total energy due to low butanol distribution of mesitylene. The energetic requirement of option 1 and 2 were 31.3 and 33.5 MJ-fuel/Kg-ABE, respectively. The energy requirement of WC column was 4.7 MJ-fuel/kg-ABE with direct bleeding. EC column for extractant regeneration operated at 1.3 bar. Heat condensation of EC was used in AC and WC boilers. With energetic integration, observed in the Figure 3-1 and 3-3, the energy requirement is reduced to 8.3 and 8.1 MJ-fuel/Kg-ABE for indirect and direct bleeding, respectively.

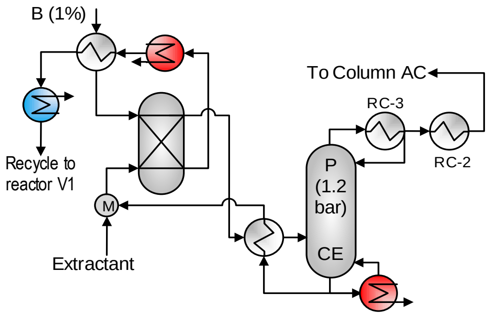


Figure 3-3. High temperature extraction configuration

In this scheme is important to mention that productivity of reactor will be not increased in ratio with conventional production because high temperature (70ºC) would kill the fermenting bacteria. This could avoid with recirculation or immobilization of biomass. However, increasing in productivity will be achieved for biomass concentration system and not for the integrated reactor. In fact, reactors with biomass concentration by recirculation or immobilization achieved the biggest productivity reported in the literature [140].

3.3.1. Dual extraction fermentation (DEx)

DEx was proposed by Kurkijärvi et al. [132] for eliminating the toxicity, in external extraction, of solvents with high distribution coefficient. In this work, an external method was proposed with recirculation option 1. In this system, 2 counter-current column extraction were used (Figure 3-4). DAL was selected as principal solvent [132]. Butanol and toxic extractant were recoveries in the first and second column, respectively. OAL was used as the biocompatible extractant for to reduce the main extractant concentration.

Kurkijärvi et al. [132] using mesitylene as the biocompatible solvent. In this work, OAL was selected in instead of mesitylene because OAL has a bigger boiling point than DAL. OAL and DAL were feed into column extraction to 3 and 8.3 kg-extractant/kg-ABE, respectively. 2.1 times less total solvent in ratio to the high-temperature scheme. Organic flow in column ExC1 and ExC2 represent 8.4 and 4.1 percent of total flow feed into column extraction, respectively.

Boiler temperatures were 272 and 239 ºC in DAL and OAL regeneration column. Condensation energy of DAL regeneration column was used to apply heat of WC boiler (Figure 3-1). The energy requirement of OAL regeneration was 0.48 MJ-fuel/kg-ABE. Without integration, total energy requirements of DEx were 22.3 MJ-fuel/kg-ABE, a decrease of 27% compared to HTE. With integration, total energy requirement was 7.1 MJ/kg-ABE. Total installation cost was $12.3MM. TAC and total installation cost of DEx were 6.4% and 8.1% lower than HTE, respectively.

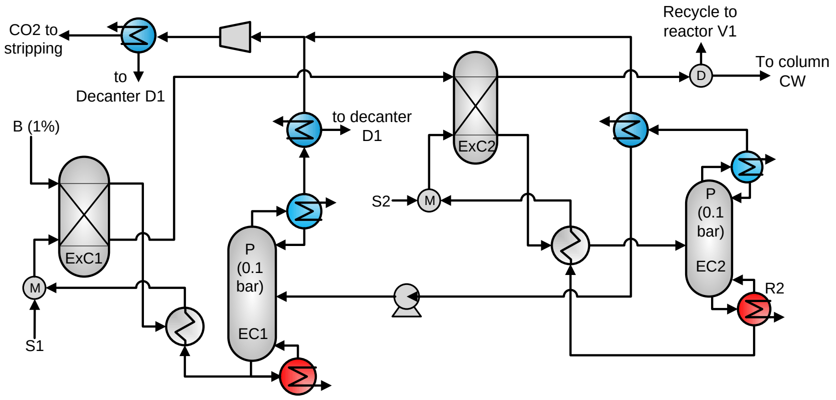


Figure 3-4. Dual extraction configuration studied in this work

Kurkijärvi et al. [132] reporting total energy requirements of 3.8 MJ/Kg-butanol or 2.5 MJ-fuel/kg-ABE (calculated in this work assuming 90% efficiency in steam production and A/B/E ratio of 3/6/1). Energy requirement was 2.8 times lower than obtained in this work. 0.47 MJ/Kg-butanol was fixed as final energy purification, supported in Kramer et al. [132] results. Bigger energy requirement achieved in this work, the same mesitylene extraction, was caused for different assumptions than for designing of a less efficient scheme.

Schemes using gasoline additives has been proposed with DEx [141]. Not product purification steps were necessaries [141]. Methyl tert-butyl ether (MTBE) and ethyl tert-butyl ether (ETBE) were the best extraction solvents. Isooctane was selected as biocompatible extractant because is non-polar and no alkanes were detected to affect the microbial growth [141]. ABE obtained in gasoline additives was 2.6%. Therefore, with this process ABE will be a minority additive in gasoline and ABE chemical market is not covered.

3.3.2. Conventional extraction with mixed extraction

In this configuration, OAL with 20 wt% of DAL has been proposed as the biocompatible extractant. OAL with 20% of DAL increased butanol distribution coefficient of 3.9 to 4.6 and reduced its boiling temperature of 272 to 209 ºC (0.166 bar). This mixture with conventional regeneration reduces energetic requirement without and with integration at 19 and 7.8 MJ-fuel/Kg-ABE, respectively. Energetic requirements with and without integration were 18% and 8.1% lower than pure OAL, respectively. Total installation cost of OAL extraction ($9.74MM) was reduced to $8.5MM using OAL-DAL mixture.

Fermentation processes with 1 extraction stage can be operated experimentally using the DAL-OAL mixture for more than 30 days [134]. In batch process productivity of reactor is around 0.5 gLh^{-1}; while, in extractive fermentation productivity with mixture extraction and bagasse of cane for cell immobilization is increasing to 2.5 $gL^{-1}h^{-1}$. In others study, extractive fermentation in fed-batch scheme productivity was increased in 70% in ratio to normal batch process [142] (without immobilization, glucose concentration of 300 g/L and oleyl alcohol as extractant); reactor productivity was increasing 2.7 times in ratio to batch process using 500 gL^{-1} of glucose and oleyl alcohol [59].

3.3.3. Direct steam regeneration

In the scheme proposed in this work, direct steam was feed to bottoms of extractant regeneration column (Figure 3-5). In this way decreased the temperature in the regeneration column reducing exchanger area in preheating. Additionally, the low operational temperature in column regeneration can prevent extractant degradation. Preheated is used to decrease direct steam flow. However, maximum temperature in column increasing proportionally in ratio to preheating (Figure 3-6).

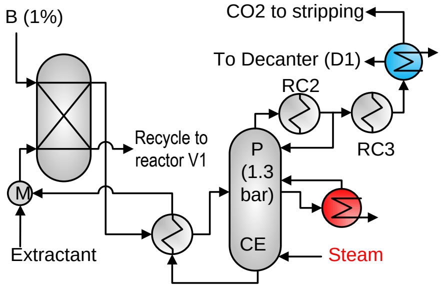


Figure 3-5. Extractant regeneration with DSD

Using OAL without energetic integration, an inflection point takes place at approximately 4.4 MJ-ABE/kg-fuel of preheating, and higher preheats generated a slight decreased in direct steam. At this preheated energy, maximum energy temperature was around 147 ºC and low-pressure steam was used. Without integration and direct bleeding, the total energy requirement for DSD was 18.1 MJ-fuel/-Kg-ABE. Energetic requirement were reduced to 6.4 MJ-fuel/-Kg-ABE with energetic integration. In mesitylene and DEx scheme, without integration, energy requirements were 1.7 and 1.2 times bigger than DSD with OAL pure extraction.

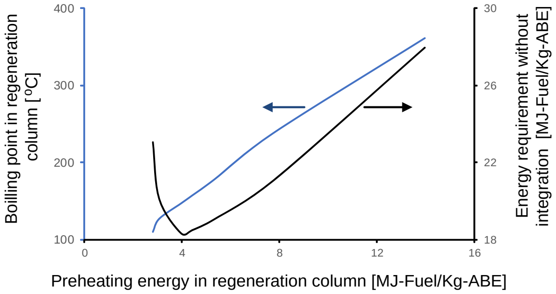


Figure 3-6. Effect of preheating in regeneration distillation column in scheme with direct steam

DSD was simulated with mixture solvents (Figure 3-7). OAL-DAL mixture was used in this work as an example. Regeneration column was proposed without condenser. DAL was partially evaporated due at low-temperature evaporation of DAL (233 ºC) in ratio to OAL (357 ºC). Therefore, an additional column was necessary to butanol purification from the extractant-butanol mixture obtained in CBE column. The minimum energy requirement of steam direct stripping without integration obtained in this work were 17.2 MJ-fuel/kg-ABE, 6% lower than DSD using pure OAL. Extractant was reduced in 16% using OAL-DAL mixture (80-20) in ratio to pure OAL.

Minimum energy requirement was obtained with a temperature and pressure feed of 168 ºC and 1.4 bar, respectively. Energy requirement were 6.8 MJ-fuel/kg-ABE with energetic integration; 0.4 MJ-fuel/kg-ABE bigger than the energetic requirement of DSD with pure OAL. DAL stripping increased temperature of CB boiler to 168 ºC. Energy requirement CB boiler and CBE column were 0.33 MJ-fuel/kg-ABE and 2 MJ-fuel/kg-ABE, respectively.

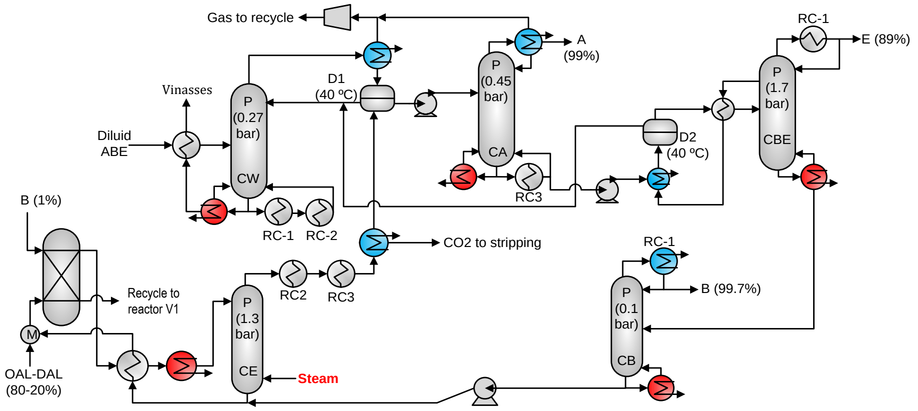


Figura 3-7. Steam direct regeneration using mixed extractants (OAL-DAL)

TAC of DSD using OAL-DAL mixture was 0.064 $/kg-ABE; 11.8% and 1.7% lowers than conventional regeneration using the same mixture and DSD using pure OAL, respectively. In the Figure 3-8 can be observed the economic performance of all configuration of extractive fermentation evaluated in this work. In the external configuration, extraction decanters cost was between 12.5 and 13.4% of TAC. With biocompatibility extractant, due reactor cost reduction, column extraction was not calculated in economic performance. TAC using DSD with pure OAL decreased in 29.4 and 33.7% in ratio to DEx and mesitylene extraction; mainly by non-cost estimation of extraction column in DSD, low heat exchanger area and fuel requirement.

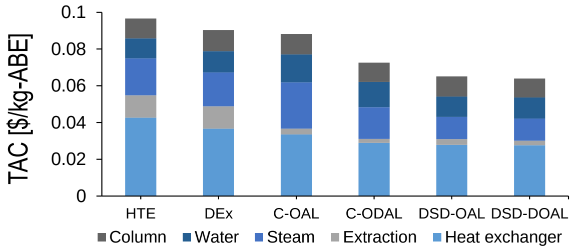


Figure 3-8. TAC of extractive distillation system evaluating in this work

3.4. Conclusions

Several systems for extractive fermentation were studied to similar assumptions. External extractions, high-temperature extraction, and dual extraction were the less economical and energetically attractive options than mixture solvents or DSD schemes. DSD was the process with the less energetic requirement and less expensive. The low energetic requirement was caused for energetic integration, which was possible for the atmospheric operation of regeneration column and the low-pressure columns used by ABE purification. The less expensive cost of DSD was caused mainly by using of biocompatible extractant and low heat exchanger area.

4. Simulation and economic optimization of hybrid reactors with vacuum evaporation or pervaporation for biobutanol production from lignocellulosic hydrolyzed

Abstract

In this paper was optimized acetone, butanol and ethanol (ABE) production from lignocellulose. The proposed reactors were simulated in Matlab® with simultaneous saccharification, fermentation and vacuum evaporation (SFS-V) or pervaporation (SFS-P). A kinetic model for ABE fermentation with hydrolyzed inhibitors was used. In the optimization, the aim function was the total annualized costs (TAC) of hybrid reactors. The final separation was performed in Aspen Plus ®. Distillation was proposed with heat integration. In contrast to literature reported, the conventional process was the choice most energetically efficient (8 MJ-fuel/kg-ABE). However, batch process was the less profitably. SFS-V using a heat-pump was the less energy efficient scheme (between 9.6-12.4 MJ-fuel/kg-ABE). TAC of SFS-V was between 1 at 5% lower than SFS-P. TAC of distillation recovery was reduced for SFS-V in ratio to conventional process in 42% for increasing in concentration. TAC of hybrid reactor decreased up to 2 times when phenolic and furans were feed at 3 gL^{-1} one each.

Keywords*:* Vacuum evaporation, membrane, double effect, compression

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4.1. Introduction

Butanol, considered a potential biofuel, is alternatively produced from biomass by acetone, butanol and ethanol (ABE) fermentation [136]. ABE fermentation is traditionally carried out by several mesophilic Clostridium, such as *Clostridium acetobutylicum, Clostridium beijerinckii, Clostridium saccharobutylicum and Clostridium saccharoperbutylicum* [1,5]. The main advantage of traditional *Clostridium* is the ability to consume a wide variety of substrates, such as glucose, sucrose, lactose, xylose, starch or glycerol [4,143]. Corn, conventional substrate, is more than 78% of total production cost in ABE fermentation [5]. The corn price fluctuates between 153-218 $/t while lignocellulosic substrates are between 24-60 $/t [144]. For these reasons and environmental concerns, ABE fermentation has been performed from several lignocellulosic substrates [28,31,33].

Butanol, considered a potential biofuel, is alternatively produced from biomass by acetone, butanol and ethanol (ABE) fermentation [136]. ABE fermentation is traditionally carried out by several mesophilic Clostridium, such as *Clostridium acetobutylicum, C. beijerinckii, C. saccharobutylicum and C. saccharoperbutylicum* [1,5]. The main advantage of clostridias is the ability to consume a wide variety of substrates, such as glucose, sucrose, lactose, xylose, starch or glycerol [4,143]. Corn, conventional substrate, is more than 78% of total production cost in ABE fermentation [5]. Lignocellulosic substrates in ratio of conventional biomass are between 3 and 5 times more economical [144]. For these reasons, and environmental concerns, biobutanol fermentation have been performed from several lignocellulosic substrates [126].

Lignocellulose requires pretreatment before enzymatic hydrolysis; which mainly reduce hemicellulose to xylose and decrease cellulose crystallinity [145]. A variety of pretreatment methods have been proposed, such as dilute acid hydrolysis, steam explosion, and liquid hot water pretreatment [146]. Glucose and xylose cause strong inhibition in enzymatic hydrolysis with high-solids loadings. Simultaneous fermentation and saccharification have been proposed to decrease product inhibition [147].

Integrated reactors with separation techniques decrease butanol inhibition, increasing ABE productivity in more than 2 times [88,148] with energy requirement between 6.3-17 MJ/kg-ABE [89]. Several separation units has been proposed, gas stripping [149], pervaporation [55], liquid-liquid extraction [150], pertraction [63], adsorption [40] and flash evaporation [64,90]. These separation units are not 100% selective, therefore, ABE is conventionally purified by distillation. After or before of ABE purification, solids in vinasses can be concentrated by centrifugation, evaporation or filtration. Finally, concentrated solids are combusted for electricity and steam production or send as cattle feed.

In this paper, was simulated rigorously a hybrid reactor with simultaneous fermentation, saccharification, and recovery. The hybrid reactors was proposed to reduce the negative effect of butanol and monosaccharides into fermentation and saccharification, respectively. Pervaporation and flash evaporation were studied in this work. Economic and energetic requirements of integrated reactor depend of several conditions and assumptions. For example, in pervaporation decreasing permeate pressure increasing reactor productivity or membrane needed; however compression work, condensation or evaporation heats are increasing. Therefore, the best operation conditions were selected by total annualized cost (TAC) minimization. Inhibitors recovery from the reactor and its effect into fermentation was studied too, because phenolic and furans are produced from lignin and hemicellulose, respectively, in pretreatment process. Pretreatment conditions not were studied in this work, for this reason, simulations were realized to several inhibitor concentrations.

Energy requirement with heat integration distillation is not as high as many scholars predicted based on the low solvent concentration (2 wt%) [129]. For example, the vapor requirement with distillation in Jilin Cathy Industrial Biotech, one of the leading butanol producers in China, is 6–7 tons/kg-butanol [129]. Therefore, energetic and economic comparison of hybrids reactor in ratio to batch process and recovery by a system of thermally integrated distillation was performed in this work.

4.2. Process Model

Simulation of simultaneous fermentation, saccharification and separation was performed in Matlab ®. The kinetic model was developed to predicted glucose and xylose consumption for *Clostridium saccharoperbutylacetonicum N1-4,* and inhibitors effect in fermentation (see supplementary info C). Experimental data of glucose and xylose fermentations were obtained from Shinto et al. [151] and Shinto et al. [152], respectively. Experimental effect of inhibitors in biocatalyst was reported by Zheng et al. [153]. An added parameter was used in furans inhibition because was observed than furans at low concentrations have non-caused inhibition in fermentation by *Clostridium beijerinckii BA101* (see supplementary info C).

Classic saccharification kinetic model was proposed by Kadam et al. [154]. Enzyme reactivity parameter was adapted for continuous operation in the transient state with changes in feed substrate concentration (see supplementary info C). In this work the word substrate was referred to the sum of cellulose and xylose. Feed ratio of cellulose/lignin/xylose was fixed to 2/1.5/1. Reactor model can be observed in supplementary info.

Vacuum evaporation (SFS-V) and pervaporation (SFS-P) schemes were simulated with in situ separation. In hybrid reactors end fermentation time was fixed to 500 h, reactor starting in batch; after of 25 h bleeding, continuous feed and butanol separation were initiated. The batch operation begins at a cellulose concentration of 30 gL^{-1} to avoid substrate inhibition. In optimization, maximum substrate concentration in continuous was fixed to 180 gL^{-1}. In all cases tested, was assumed not loss of substrate in butanol concentrated phase.

UNICUAC parameters in its majority were taken of Aspen Plus® for Matlab® simulation. Only butanol-water binary parameters were taken from Fisher and Gmehling et al. [135]. Furans and phenolic compounds effect in economical optimization were studied feed furfural and vanillin into reactor, respectively. In pretreatment was supposed that hydrolyzed were obtained to 180 g-substrate/L in all cases tested. Therefore, if the substrate concentration was less than 180 gL^{-1} in optimization, hydrolyzed was diluted. Water dilution cost was disregarded. Optimization and minimization in the kinetic model were performed with Matlab® functions 'ga' and 'fminsearch'. TAC was the objective function in optimization.

Annual operational time and time of return on investment were 8150 h and 3 years, respectively. The energetic evaluation was calculated assuming an efficiency in steam and electricity production of 0.9 and 0.33, respectively. The isentropic efficiency of the compressor was 0.75. Compression system was performed in 4 stages. Pressure drop in condensation was fixed to 0.03 bar. Heat reaction was assuming null. The simulation was performed with approach temperature of 10 ºC. Occupation volume of the reactor was fixed to 0.8. Maximum volume reactor was 1000 m^3. The global coefficient heat was fixed to 284, 568 and 852 $W/s/m^2$ for partial condensation in CO_2-liquid evaporation, liquid heat-liquid heat and vapor condensation-liquid evaporation respectively. Investment equipment functions were taken from Douglas et al. [114]. The reactor function cost was reported by Oudshoorn et al. [79]. Low pressure steam, cool water, electricity, enzyme costs were 2.18 \$/ton-steam (3 atm) [139], 0.06 \$/ton-water, 0.1 \$/kWh and 4.3 \$/kg-protein, respectively. Production flow was 4000 kg-butanol/h. Only reactor and ABE recovery cost were evaluated in this work.

4.2.1. Evaporation

In SFS-E CO_2 compression was performed with a heat pump to increase the energy efficiency. A heat pump allowed to use condensation heat of compressed vapor to give energy to its evaporation (Figure 4-1). Then, the total energy requirement of SFS-E was given for compression work. The hybrid scheme was simulated in Aspen plus® with a stoichiometric reactor (RStoic) and flash separator (Flash2), for validate SFS-E model developed in Matlab®. The optimization variables were: dilution rate, enzymes ratio, vacuum pressure, substrate concentration and work at each stage of compression.

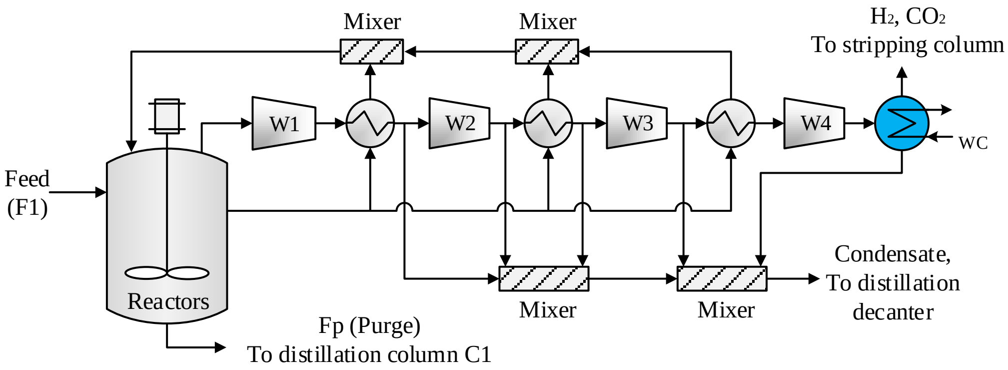

Figure 4-1. Simultaneous fermentation, saccharification and flash evaporation with a heat pump (SFS-V) proposed with 2-stage condensing

4.2.2. Pervaporation

In this work, membrane fouling was depreciated. However, in the reactor with high solids loading nanofiltration or microfiltration before pervaporation can be necessary [155]. In the literature, experiments are conducted at pressures lower than 2 mbar. Knowing the flux, the compositions and temperatures at which the experiments were carried out, and assuming that the vacuum pressure was equal to 0 membrane permeance was determined by the following equation:

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$$Per_i = \frac{J_i}{\left(x_i \cdot \gamma_i \cdot Psat_i\right)} \tag{4-1}$$

Membranes with higher permeances or selectivities reported in the literature can be found [51,156–161] in Table 4-1. Permeance and selectivity were assuming constant [162]. Only CO_2, H_2 and water selectivities were assuming 1. Otherwise, selectivity was equal to butanol selectivity. An optimistic membrane life time was assuming. Membrane life was 3 times lower than conventional equipment. In this work, a low installed membrane cost was used (100 \$/m^2 module costs were included). CO_2 compression was realized in multistage. Condensation was performed to 30 ºC. A heat pump was not proposed by the low pressure of permeate and high membrane selectivity.

In optimization, was assumed that condensation heat in distillation was enough to apply heat to evaporation in reaction. Therefore, the energetic requirement of the hybrid reactor was the compressor work. This supposition was counteracted after optimization, in the evaluation of distillation scheme. Scheme of SFS-P can be observed in the Figure 4-2. The variables to be optimized were: Feed flow, permeate pressure, enzymes concentration, substrate concentration and compressor works.

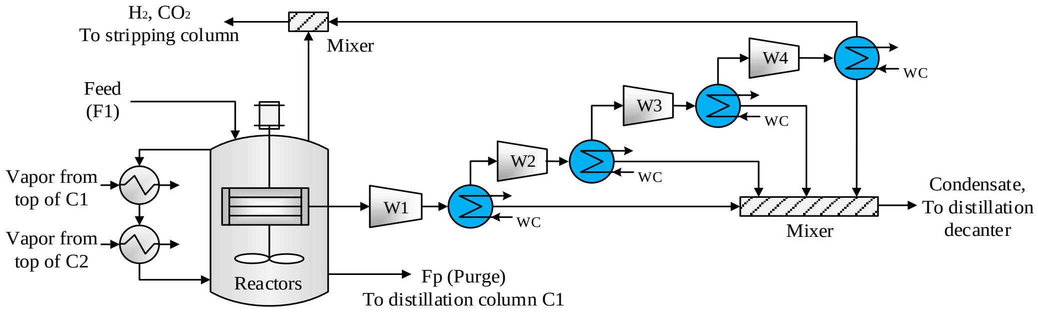


Figure 4-2. Production scheme with simultaneous fermentation, saccharification and pervaporation (SFS-P)

Table 4-1. Membranes reported in the literature for the separation to butanol

Membrane	Temperature [C]	Mass fraction	Flux [kgm^{-2}h^{-1}]	Separation Factor	Permeance [molbar^{-1}m^{2}h^{-1}]	Selectivity
PTMSP [156]	25-70	0.01	0.06-1.0	52-70	159-334	2.3-3.2
Silicalite-PTMSP [157]	*50*	*0.05*	*9.5*	*106*	*4061*	*6.2*
Silicalite-PDMS [158]	80	0.002-0.03	5-11.2	41.6-25	990-1009	1.9-1.3
Silicalite-PDMS [51]	30-70	0.01	0.06-0.61	86-93	167-240	3.8-4.3
PDMS-ceramic support [159]	*40*	*0.01*	*1.28*	*42.9*	*1285*	*1.9*
OA/PP [160]	30	0.0095	0.08	180	29.1	8.4
TOA/PP [161]	*54*	*0.015*	*0.053*	*240*	*47.2*	*11.2*

PP, polypropylene. OA, oleyl alcohol. TOA, trioctylamine. PDMS, polydimethylsiloxane. PTMSP, poly[1-(trimethylsilyl)-1-propyne]

4.2.3. Distillation

ABE purification by distillation was simulated in Aspen Plus® after getting the optimal reactor conditions. Acetone, butanol and ethanol purity achieved in simulations were 0.99, 0.9 and 0.997 respectively. ABE recovery was fixed to 0.975. The configuration used in this work was a double-effect distillation with 4 separation columns (Figure 4-3). Decanter was simulated with parameter of liquid-liquid equilibrium. The plates of C1-LP, C1, C2 and C3 columns were 19, 38, 28 and 14 respectively. Intermediate condensation heater of column C1 was used to supply heat to the reboiler of low-pressures columns (C1-LP and C2 columns).The concentrated butanol phase was fed directly to the decanter. Non-condensables (CO_2 and H_2) were sent to a stripping column (10 plates) to recover carried ABE.

4.3. Results and discussion

4.3.1. Kinetic model

The model proposed in this work improve mean correlation coefficient of all metabolites of 0.9 to 0.93 and decreased the average error of final concentration of butanol and acetone of 10% and 14% to 3.4 and 8.3%, respectively, regarding Shinto et al. [151] model. Mean error with inhibitors in butanol and ABE prediction were 13% and 7.9%, respectively. High error in the model was considerate acceptable in this work because media variability in hydrolyzed experimental fermentations for ABE and butanol production are 13.2 and 15.3%, respectively [153]. Greatest phenolic and furan concentration that inhibits the growth, in minimization, was 2.9 g/L and 4.1 g/L, respectively. Experimental study of nutrients supplementation and individual inhibitors effects in *Clostridium saccharoperbutylacetonicum N1-4* must be realized to get a better predictive model.

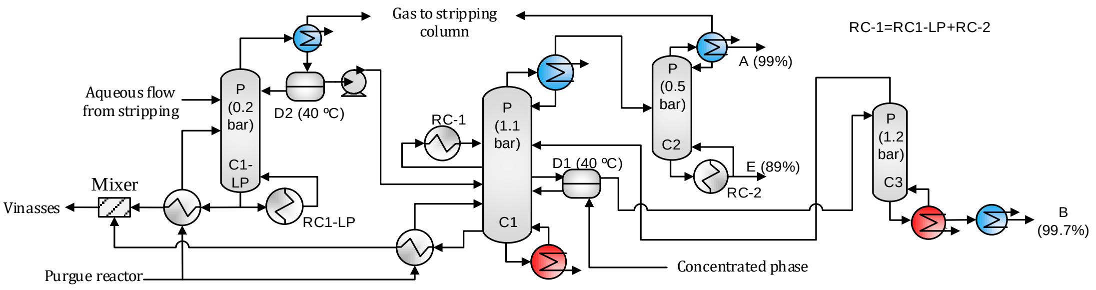


Figure 4-3. Scheme of multiefect-distillation by acetone, ethanol, and butanol purification (S-I)

4.3.2. Optimization of SFS-V

Matlab® simulation was compared with Aspen Plus® simulation for model validation. Glucose conversion, vacuum pressure, and compressor works were fixed in Aspen Plus® from optimal conditions (feeding only glucose at 180 g-glucose/L and 0.06 \$/kg-glucose). Butanol concentration into reactor, ABE in vapor phase, total compressor work and evaporation heat in contrast to Matlab® simulation, had an absolute deviation percentage of 0.7%, 0.9%, 4.8% and 4.4%, respectively, regarding Aspen Plus® simulation. Butanol/acetone/ethanol ratio in optimal conditions was 9.7/5.5/1.

ABE ratio using lignocellulosic hydrolyzed (hydrolyzed cost: 0.06 \$/kg-substrate) was 13.7/2.8/1. Experimental butanol/acetone production reported by Shinto et al. [152], for *Clostridium saccharoperbutylacetonicum* N1-4 for 9.5 and 53.5 g-glucose/L were 4 and 2, respectively. While experimental butanol/acetone ratio using xylose were between 4 and 6.1 [151]. Therefore, butanol/acetone ratio using glucose (1.8) and lignocellulose (4.9) was realistic in contrast with experimental data.

TAC in optimal conditions were between 0.42 and 0.81 \$/kg for substrate costs between 0.03 and 0.15 \$/kg (Figure 4-4). In ratio to batch process (simultaneous fermentation and saccharification) to optimal conditions (substrate cost of 0.06 \$/kg) TAC was reduced in 22%. Vacuum pressure was between 0.047 and 0.056 bar. Heat pump had the coefficient of performance (COP) between 4.8 and 6.5 (evaporation heat requirement divided by total compression work). This low COP was due mainly to CO_2 and H_2 compositions in the vapor phase. The heat pump was considerate the best option for energetic integration because non-condensable (CO_2 and H_2) must be comprising at atmos. pressure.

Energetic requirement were increasing in optimal conditions with higher substrate cost; for to obtain higher yield without to diminish reactor productivity (Fig. 4). Yield was increasing of 0.25 to 0.35 g-ABE/g-substrate with increasing of a substrate cost of 0.03 to 0.12 kg-ABE/kg-substrate; while compressor work was increasing of 5.5 to 9.9 MJ-fuel/kg-ABE. Simulation with optimal conditions obtained with a substrate cost of 0.03 \$/kg-ABE was performed with a substrate cost of 0.15 \$/kg-ABE without optimization. TAC with this substrate cost and conditions was 0.91 \$/kg-ABE; 13.7% higher than TAC obtained with optimization at 0.15 \$/kg-ABE. This reduction was performed with an increasing of work requirement of 1.8 times. Otherwise, compression work was rising between 10-15% when pressure drop was increasing of 0.03 to 0.12

bar. TAC in optimal conditions was increasing between 6.2 and 7.4% with pressure drop increment.

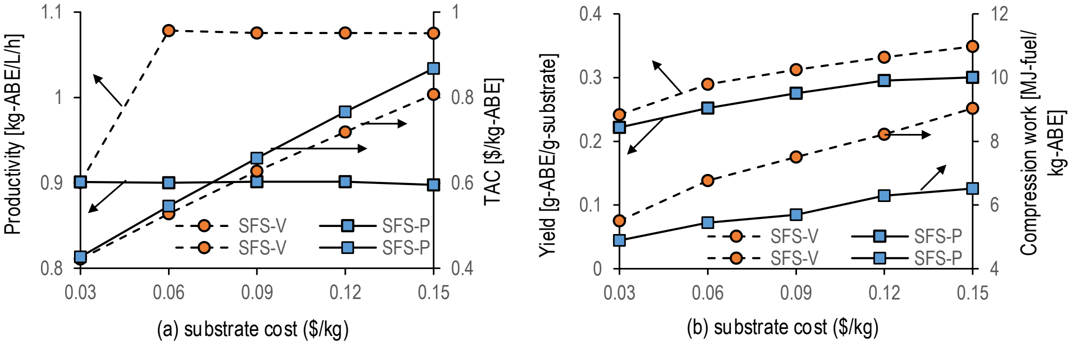


Figure 4-4. Effect of lignocellulose hydrolyzed cost in TAC, productivity, work compression and yield in simulation with economical optimum conditions for SFS-V and SFS-P (PTMSP membrane)

Reactor productivity in optimal conditions was 0.9-1.1 g-ABE/L/h. Mariano et al. [65] proposed butanol productivity for a fixed substrate conversion as objective function of optimization. These objective function returns confuse with lignocellulose substrate because was necessary another optimization restriction enzyme fed. Additionally, compressor works not can be optimized and increasing reactor productivity need more energetic requirements.

4.3.3. Optimization of SFS-P

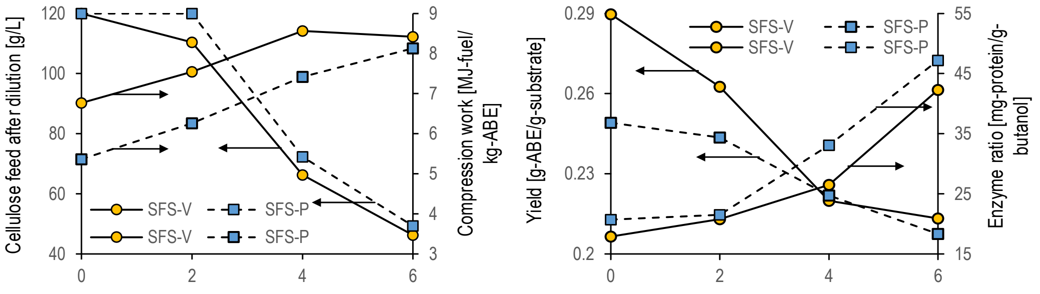
Temperature can be increased in external units and improve pervaporation performance. However, external units with temperature increasing was not studied in this work by the following two reasons: 1) Increases the equipment number that should be used, like biomass recirculation or immobilization units and heat exchanges 2) Need large energy requirements by low solvent concentrations into reactor; for example, energy consumption to raise 10 ºC a stream with butanol concentration of 5 and 10 gL^{-1} were 8.7 and 4.4 MJ/kg-butanol respectively.

Several membranes have been reported by butanol recovery [51,156–161] (Table 4-1). In this work, composite membrane silicalite-PTMSP was selected for the optimization by its high permeance and selectivity. TOA/PP was selected by its high selectivity (11). PDMS-ceramic support was studied because had intermediate permeability and selectivity (1.9) (Table 4-1). Experimentally, TOA/PP [161] and PDMS [159] membranes were operated for 300 and 200 h without significate changes in performance, respectively. Stability of silicalite-PTMSP membrane is unknown. Long term testing of stability are required for this membrane because difficult polymer synthesis and membrane stability issues are impeding in the upscaling of the manufacturing of PTMSP membranes [163]. However, PTMSP membrane was studied in this work as optimistic membrane.

Membrane area was increasing of 7100 to 15000 m^2 with substrate cost increasing of 0.03 to 0.15 $/kg, respectively. TAC of SFS-P with silicalite-PTMSP, TOA/PP and PDMS were 0.55, 0.73 and 0.62 $/kg-ABE, respectively (substrate cost: 0.06 $/kg-ABE). Interestingly, membrane area required in optimal conditions using TOA/PP was null. Therefore, optimum conditions of TOA/PP membrane was equal at the not integrated reactor in semi-continuous mode. Membrane area of PDMS was 2.3 times higher than PTMSP. Heat requirement of evaporation for PTMSP and PDMS were 2.3 and 3.9 MJ/kg-ABE, respectively. This vaporization energy was 78% and 64% lower than SFS-E in optimal conditions. Compressor works by PTMSP and PDMS membranes in optimal conditions were similar (18% lower than SFS-E), because less productivity was achieved in optimization with PDMS membrane.

In the literature, the energy requirement of pervaporation is associated to low heat evaporation for its high selectivity [67,87]; however compression work of CO_2 was the item more important in energy requirement calculation. Compression energy was 3.8 MJ-fuel/kg-ABE while heat evaporation into reactor was 2.3 MJ/kg-ABE (PTMSP-membrane). Butanol fraction in vapor phase of high selectivity membrane and low temperature fermentation decreases the force guide for pervaporation. Therefore, low pressure (8.2 mbar) was needed. Higher enzyme load (36.2 g-protein/kg-butanol and PTMSP-membrane) than SFS-E (26 g-protein/kg-butanol) was needed by membrane area cost. TAC for PTMSP-membrane was between 1 and 7.5% higher and work requirement was between 11 and 28% lower than SFS-E.

Pervaporation or evaporation was not an efficient way for hydrolyzed inhibitors recovery and in the optimization was necessary decreasing substrate concentration to diminish inhibitors concentration in the fed (Figure 4-5). Therefore, higher recovery cost in distillation, pretreatment and solids separation must be necessary. Additionally, compression work was increasing of 1.7 to 1.9 MJ-fuel/kg-ABE for SFS-P. Hydrolyzed inhibitors recovery was difficult by its high boiling point. In all cases, SFS-E achieved higher yield, lower productivity and higher energy requirement than SFS-P (Figure 4-5). TAC of SFS-P was increasing in 15% and 53% at hydrolyzed inhibitors concentration of 2 and 4 g/L, respectively. Hydrolyzed inhibitors increasing TAC to 2 times with inhibitors concentration of 6 gL^{-1} (substrate cost: 0.06 \$/kg-ABE).



(a) Inhibitor concentration in hydrolysed (g/l) (b) Inhibitor concentration in hydrolysed (g/l)

Figure 4-5. Effect of inhibitor concentration before dilution in substrate fed after dilution, enzyme ratio, work compression and yield in simulation with economical optimum conditions for SFS-V and SFS-P (pervaporation)

4.3.4. Energetic evaluation and distillation cost

The acetone unrecovered was obtained mainly in the non-condensable gas. While ethanol and butanol unrecovered was founded in vinasses. Only 0.1% of butanol was unrecovered. Heat requirement and TAC of distillation units for non-integrated reactor were 0.139 \$/kg-ABE and 8 MJ-fuel/kg-ABE, respectively. In the literature, energetic requirements by distillation have been reported between 18 and 21 MJ/kg-ABE [89,124,164]. Low energetic requirement obtained in this work by distillation was caused by intensive energetic integration and more efficient configuration. Higher integration was obtained in preheated of distillation units (14 MJ/kg-ABE). While, recovery in condensation-reboiler, RC-1 (Fig. 3), was 3.7 MJ/kg-ABE.

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The energy requirement of distillation for SFS-V and SFS-P was around 4.1 MJ-fuel/kg-ABE, 48% lower than conventional because ABE concentration was increasing in 4.7 times (optimal conditions: substrate cost 0.06 $/kg). In consequence, the separation cost of distillation was 42% or 46.8% lower for SFS-V or SFS-P, respectively. Distillation cost of SFS-P was 0.064 $/kg; 7.4% lower than SFS-V because needed lower water cold (condenser heat was used to supply heat to the reactor).

Total energy requirements of SFS-P was 9.5 MJ-fuel/Kg-ABE (optimal conditions at 0.06 $/kg-substrate); 19% higher than conventional distillation and 12% lower than SFS-V. The energy requirement of distillation was reduced of 4.2 to 3.6 MJ-fuel/kg-ABE when ABE yield was increasing (optimal conditions at 0.15 $/kg-substrate); however, total energy requirement was increasing of 9.5 to 10.1 MJ-fuel/kg-ABE for increasing in water evaporation and gas compression. Similar energy consumption has been reported for pervaporation in the literature, 9 MJ/kg-ABE [66] and 14 MJ/kg-butanol or 10.9 MJ/kg-ABE (calculate in this work with *C. beijerinkii BA101* solvent yield) [89]. However, the implication of compression work of CO_2 in these reports is not clear.

Energetic requirement obtained for SFS-V in this work was 1.66 times lower than Mariano et al. [124] reported (18 MJ-fuel/kg-ABE; calculated with energy efficiencies from this paper). Compression work reported by Mariano et al. [124] is 5.5 MJ/kg-butanol or 3.7 MJ/kg-ABE. In this work, the energy requirement for compression was between 1.6 and 2.7 MJ/Kg-ABE, under optimal conditions at a substrate cost between 0.03 and 0.15 $/kg-ABE. The compression work was lower due to different suppositions (ABE yield, ABE ratio, ABE concentration into reactor and pressure drop), optimization and more efficient compression scheme (4 compressor instead of 2). The energy requirement of distillation (5 column system) reported by Mariano et al. [124] is 6.5 MJ-fuel/kg-ABE [124], 58% higher than the energetic requirement reported in this work.

4.4. Conclusions

A heat pump was an efficient way for heat recovery in flash evaporation due to CO_2 compression. TAC and energy requirements of the PTMSP-ceramic membrane were between 1 to 7.5% higher and 11 to 28% lower than SFS-V. PTMSP reduced the TAC regarding of PDMS membrane between 12 to 17%. However, stability of PTMSP membranes is lower than PDMS membranes, and this effect not studied in this work. High selective membrane, TOA, not was a better choice than continuous fermentation process without simultaneous recovery by its low permeability. SFS-E and SFS-P performances were reduced 2 times with addition of 9 gL^{-1} of hydrolyzed inhibitors concentration. The direct heat integration distillation system was the most efficient energetically and the less profitably option. An effective detoxification method must be used if SFS-E or SFS-P is applied in industrial scale for butanol manufacture from lignocellulose.

5. Optimization of simultaneous butanol fermentation and detoxification by liquid-liquid extraction

Abstract

In this paper, acetone, butanol and ethanol (ABE) production from lignocellulosic biomass was simulated and economically optimized. The reaction system was carried out with simultaneous saccharification, fermentation, and liquid-liquid extraction. Optimization of the integrated reactor was performed in Matlab®. In Aspen plus® was studied the distillation system. The detoxification effect in fermentation with oleyl alcohol (OAL) was studied with a kinetic model to several concentrations. The total annualized cost (TAC) achieved by mixed extraction (2-ethyl-1-hexanol/oleyl alcohol to 10:90) was 7.8% lower than pure OAL extraction. However, the low boiling point of 2E1H not allowed simultaneous detoxification. TAC of the detoxification system in a ratio to batch process and dilute concentrations was 45% lower. Also energetic study of a thermally integrated distillation system was performed.

Keywords: detoxification; ABE fermentation; oleyl alcohol; 2-ethyl-1-hexanol; extractive fermentation

Paper under review

5.1. Introducción

Biobutanol is an attractive biofuel with better properties than ethanol and a high demand annual as chemical [5]. Has been produced mainly by several clostridia [5]. Lignocellulose is the most abundant renewable resource by biobutanol production. Sugars from lignocellulosic substrates can be obtained by an enzymatic way, however, a pretreatment is necessary due to the high grade of polymerization of biomass [146]. In the pretreatment, several inhibitors of fermentation are produced. Ratio and concentration of these inhibitors depend on parameters pretreatment and scheme selected [165].

Substrate dilution and detoxification methods are proposed to reduce these inhibitors. Detoxification methods before fermentation include extraction, adsorption, evaporation, electrodialysis, over-liming, neutralization, steam stripping, enzymatic or microbial treatment [166]. The extractive fermentation can be used to remove phenolic compounds, furans, and butanol and better the performance of the reactor. However, extraction need high-boiling solvent due to the boiling point of furans derivate or phenolic compounds.

Coumaric and ferulic acid, major products of lignin degradation, has a boiling point of 316 and 405 ºC, respectively. Phenolic compounds are the most toxic compound to biocatalyst, for instance 0.5 gL^{-1} of ferulic acid inhibit totally ABE production of *Clostridium beijerinckii BA101* [143] and decreased the growth of *C. beijerinckii NCIMB 8052* in 30% with solvents reduction of 14 to 11.7 g/L [167]. Oleyl alcohol (OAL), the most studied extractant in the literature for biobutanol production by its biocompatibility, has a boiling point of 357 ºC to atmospheric pressure. Therefore, coumaric acid recovery is difficult and ferulic recovery in the top by distillation is impractical.

Clostridia species, advantageously, are able to transform these phenolic acids to molecules with a low boiling point. For example, p-coumaric acid is converted to p-hydroxyl-hydrocinnamic acid by reduction or to 4-vinylphenol and then 4-ethylphenol [165]. 4-Hydroxyl-hydrocinnamic acid, 4-vinylphenol, and 4-ethylphenol have a boiling point of 285, 229 and 218 ºC, respectively. Therefore, extractant regeneration by distillation is becoming more feasible. In *Clostridium beijerinkii NCIMB 8052*, 100% of coumaric acid, furfural and HMF and 8.7% of ferulic acid are consumed in less than 12 hours [165]. Furfural and HMF are reduced to furfuryl alcohol and 2,5-bis-hydroxymethylfuran (2,5-DMF), respectively [165]. Furfuryl alcohol is the main commercial chemical derivate from furfural. In this work, was optimized with a predictive model a detoxification system with simultaneous fermentation and extraction.

The scheme proposed in this work include extractant regeneration by distillation with partial extractant evaporation and intensive energetic integration (Figure 5-1). The minimum cost of selling for furans and phenolic compounds, minus its purification cost, to equal the economic potential of a mixed extraction system without inhibitors supplementation, was determined after optimization.

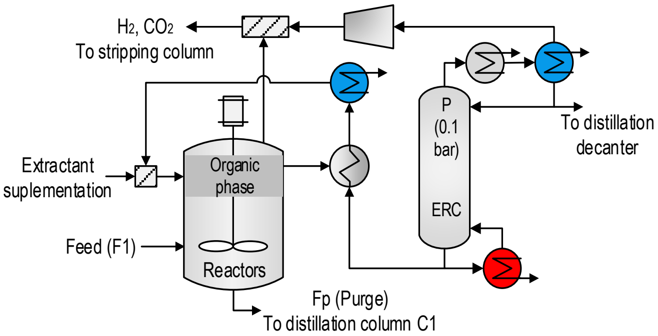

Figure 5-1 Integrated reactor with liquid extraction system

5.2. Process model

5.2.1. Kinetic model

Simulation of hybrid system was performed in Matlab ®. The fermentation model was developed by *Clostridium saccharoperbutylacetonicum N1-4* (see supplementary info C). The model was included the effect of hydrolyzed inhibitors in biomass growth. The experimental data were taken from [153]. The metabolic model proposed by Shinto et al. was modified for improve the correlation coefficient of all metabolites of 0.9 to 0.93 and decreased the average error of butanol and acetone in final concentration prediction of 10% and 14% to 3.4 and 8.3%, respectively (Figure 5-2). The Final error prediction of ABE and butanol concentration with inhibitors from the model were 8.3% and 13%, respectively. Saccharification kinetic model was proposed by Kadam et al. The Enzyme reactivity parameter was adapted for continuous operation in the transient state with a change in substrate loading (see supplementary info D).

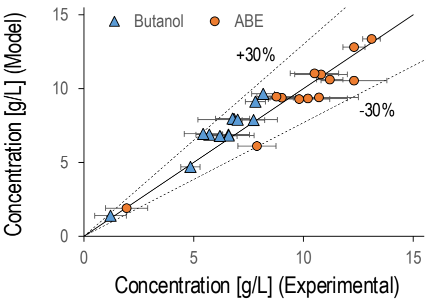

Figure 5-2. Parity diagram of butanol and ABE prediction by kinetic model. Experimental data from Zheng et al. [153]

5.2.2. Thermodynamic model and extractant selection

The extractants used in mixed extraction were 2-ethyl-1-hexanol (2E1H) and oleyl alcohol (OAL). OAL was selected because is the conventional biocompatible extractant used in the literature. OAL has a medium partition coefficient (3.8 [168], 4.6 [169]), high selectivity (295 [169], 330 [131]) and high boiling temperature (357 ºC). 2E1H was selected by its high partition coefficient ((8 ± 1.5 [169]), high selectivity (311 ± 62 [169]), low cost (1.1 $/kg [138]) and medium boiling temperature (185 ºC). Pure OAL was used as an extractant for simultaneous detoxification by its high-boiling point.

The majority of UNICUAC binary parameters for equilibrium liquid-liquid and equilibrium liquid-vapor (ELV) in simulations were taken from Aspen Plus®, the missing parameters were calculated by UNIFAC. OAL-water parameters were adjusted from UNIFAC-LL equilibrium prediction from Aspen Plus®. Butanol-water binary parameters used in Aspen Plus® and Matlab® for VLE was reported by Fisher and Gmehling et al. [135]. Van der Merwe [170] and Liu et al. [171] reported external extraction with 2E1H assuming infinite selectivity. In this work, UNIQUAC binary parameters for acetone, acetic, butanol, water and 2E1H (supplementary info) were obtained by error minimization of prediction in ratio to experimental data reported in the references [172–175]. The parity diagram of concentration was illustrated in the Fig. A-1 (supplementary info).

In the simulations were selected vanillin (VaN) and furfuryl alcohol (FuOL) as phenolic and furan compounds, respectively. VaN, FuOL, and acetic acid were feeding to the reactor at the same concentration in all cases evaluated. VaN was selected as mean properties compound because has a high boiling point (285ºC); higher than conversion products of coumaric acid. Additionally, solubilized lignin is simulated in the literature as VaN [176]. FuOL was selected because was assumed total conversion of furfural. VaN and FuOL extraction by OAL were performed using conservators and constants distribution coefficients of 1 and 3, respectively (Table 4-1).

5.2.3. Fermentation system and optimization method

Fermentation time was fixed to 500 h, the reactor starting in batch at a cellulose concentration of 20 gL^{-1}. Bleeding, continuous feed, and butanol separation were initiated after of 20 hours. Cellulose concentration in continuous operation was 120 gL^{-1} in all cases. In pretreatment was supposed that hydrolyzed inhibitors were obtained to 120 g-cellulose/L in all cases tested. Therefore, the substrate was diluted when its concentration was less than 120 gL^{-1}. The water dilution cost was disregarded. The working volume of each reactor was assumed as 0.8. The maximum volume of reactors was 1000 m^3. The total flow of renewable resource was 25000 ton/kg-dry-lignocellulose. In this work, substrate word was referred to the sum of cellulose and xylose.

Table 5-1. Partition coefficient of solvents in oleyl alcohol (*350 ºC)

Solvent	Partition coefficient	
	Experimental	UNIQ-2
Butanol (*119 ºC)	3-4	3.9
Acetone (58 ºC)	0.34	0.48
Ethanol (* 79 ºC)	0.2-0.3	0.29
Acetic acid (*118 ºC)	0.15-0.2	0.05
Butyric acid (*163 ºC)	-	2.2
Furfural (*162 ºC)	1.49-1.5	1.2
Vanillin (*285 ºC)	5.6-7.1	11.8
HMF (*291 ºC)	0.24-0.26	0.05
2,5-DMF (*275 ºC)	-	0.51
Furfuryl alcohol (*170ºC)	-	2.6
Coumaric acid (*316ºC)	-	10.6
Ferulic acid (*405ºC)	-	4.4

*Boiling point temperature

The column diameter; heat and reboiler, condenser and exchanger temperatures were determined in Aspen Plus®, previously at the optimization. A sensitivity analysis was performed based on the ratio of extractant/solvents. These data were adjusted to the ratio of extractant/solvent between 12 and 80 or 160 kg-Extractant/kg-solvent for mixed and OAL extraction, respectively. The objective function to maximize was the total annualized cost (TAC), at a fixed time of return on investment (t_{ri}), of integrated reactor and extractant regeneration system (Figure 5-1).

The cos of sell of butanol, acetone, ethanol and butyric was 1, 0.7, 0.8 and 2 $/kg, respectively. OAL and 2E1H had a cost of 4.3 and 1.9 $/kg [138], respectively. The total purchase cost of the extractant, due to recycling, was the extractant flow in the continuous state plus the extractant occupation in the reactor, and the equipments necessaries for the extractant regeneration (heat exchanger, boiler, condenser, column, etc.). Residence time in regeneration and reactor system was assumed as 3 hours, therefore the extractant was 4 times higher than the simulated in the continuous state.

5.2.4. Distillation system

The energetic evaluation was calculated assuming an efficiency in low steam, medium steam, high steam and electricity productions of 0.9, 0.85, 0.8 and 0.33, respectively, after of obtaining the optimal conditions of the reaction system in Matlab® (Solvent flow and equivalent dextrose concentration and conversions). Simulations were performed with an approach temperature of 10 ºC. In mixed extraction was proposed an intensive method of thermally integrated distillation using dual-effect distillation and high-low-pressure concept (condensation heat of high-pressure column is used in the boiler of low-pressure columns).

The configuration was proposed with 5 distillation columns. The plates of “1”, 2-LP (0.3 bar), 2–HP (1.3 bar), “3”, “4” and “5” (0.5 bar) columns were 13, 19, 19, 19, 18 and 9 trays, respectively (Figure 5-3). The intermediate condensation heater in column “3” was used to supply heat to the reboiler of 2-LP and “5” columns. The concentrated butanol phase is fed directly to the decanter of 2-LP column. Non-condensables (CO_2 and H_2) were feed to a stripping column (10 plates) to recover carried ABE. The regeneration column “1” operates at 0.1 atm in the top to prevent extractant degradation. The trays number was 13.

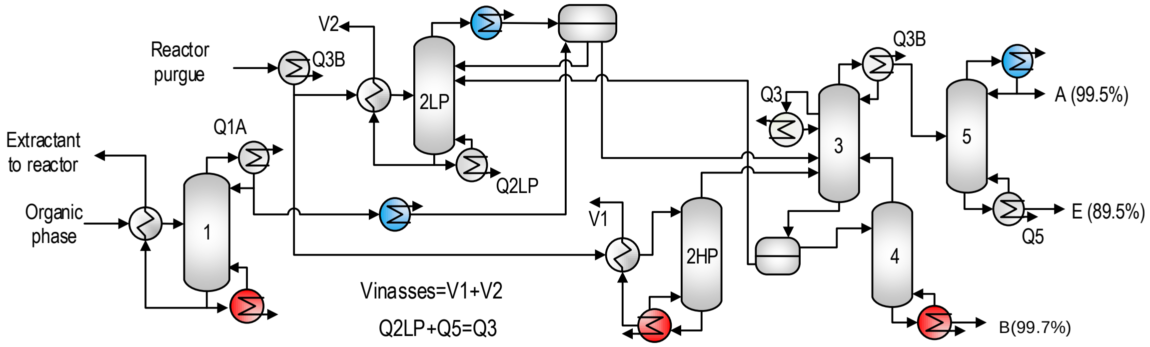

Figure 5-3. Distillation system with extractant regeneration to vacuum and double-effect heat integration

A distillation system was proposed for simultaneous detoxification, using the partial extractant evaporation in the regeneration column for the azeotropes and improve the heat integration. Fortunately, butanol azeotropes with furans, phenolic compounds, extractant or butyric acid were not formed. Additionally, the majority of azeotropes can be broken by decantation. OAL increasing the selectivity of decantation reducing the energetic requirement of distillation system. The distillation system proposed in this work was designed to obtain butanol, acetone, and ethanol to 99.7, 99.5, and 89 wt%, respectively (Figure 5-4).

Butyric acid was obtained to 99.7 wt% in OAL extraction without furfuryl alcohol supplementation. In otherwise, this was found in a mixture with FuOL, VaN, and OAL. OAL was not recovery totally because was found an azeotrope between vanillin and OAL (~15-23 wt% of OAL). The OAL loss cost in the top was not calculated, because was estimated the minimum sell cost for VaN and FuOL, minus the cost of its final separation and OAL recovery necessary to equal the economic potential of mixed extraction without detoxification.

5.3. Result and discussion

5.3.1. Optimization of SFS

SFS was simulated in batch. The variables of final optimization were fermentation time, and enzymes and cellulose concentrations. The hydrolyzed Inhibitors concentration was reduced by water dilution. However, water dilution cost was not calculated. At a substrate cost of 0.08 \$/kg-substrate and non-inherent inhibitors the optimal conditions were 49.2 h, 48 g-protein/kg-butanol and 39.5 g-cellulose/L for fermentation time, total enzyme ratio and cellulose concentration, respectively. A productivity of 0.35 g-ABE $L^{-1}h^{-1}$; ABE yield of 0.286; acetone, ethanol and butanol concentrations of 4, 1 and 11.6 gL^{-1}, were achieved in the fermentation simulation, respectively.

Substrate cost, enzyme cost and reactor cost were 38.9%, 19%, and 41.5% of TAC, respectively. Economical potential (EP) without separation cost was reduced of 7.8 to 2.2 MUSD/year with increasing in the substrate cost of 0.08 to 0.12 \$/kg. In optimal conditions, EP was reduced in 52% (0.12 \$/kg-substrate) with hydrolyzed inhibitors in the pretreatment to

3 g/L (VaN, FuOL, and acetic acid to 1 g/L each one).

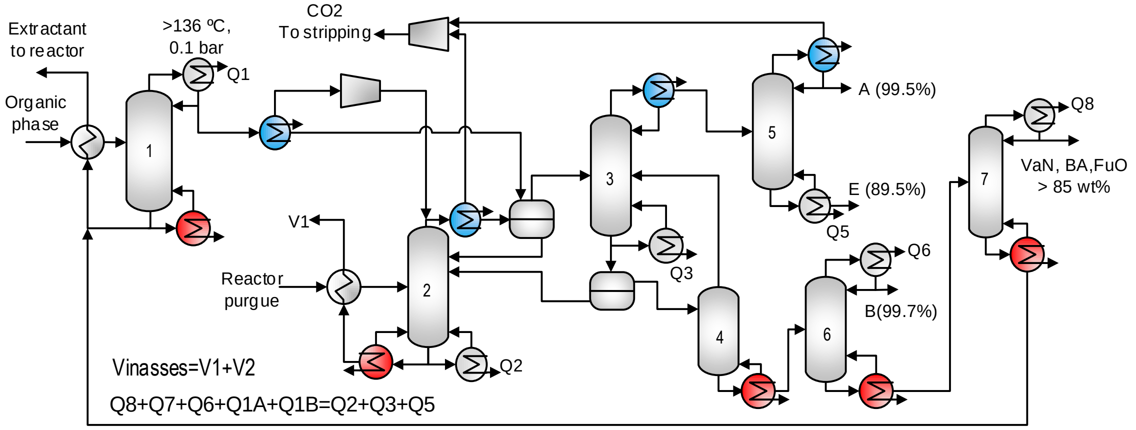

Figure 5-4. Distillation system with partial OAL loss in the top of extractant regeneration column and heat integration

5.3.2. Optimization of extractive fermentation with mixed solvent (SFS-Ms)

A mixed solvent of toxic and non-toxic extractant allow increasing the solvent distribution coefficient, decreasing the boiling point or increasing selectivity of the extractant. However, the mixed ratio is limited by its toxicity [134]. The toxicity of extractant can be estimated with log P method. In Log P method solvent distribution coefficient in octanol/water mixed is calculated. Higher polarity or lower Log P imply higher toxicity of extractant. Molar Log P of 2E1H and decanol was 2.8 and 4.3, respectively. Therefore, 2E1H was more toxic than decanol.

The butanol productivity was increasing in more than 2 times using 20/80 Decanol/OAL mixture [134]. In this work, due to higher toxicity of 2E1H, 10:90 2E1H/OAL ratio was used. Butanol distribution coefficient and the selectivity calculated with UNIQUAC were 3.8, 338, and 8.1, 340 for OAL and 2E1H, respectively. Using OAL/2E1H mixture butanol distribution and selectivity were increasing at 4.8 and 392, respectively. Sensitivity analysis was performed to determinate sizing functions for economic optimization (Table 5-2). Extractant loss in the top was fixed to 0.01 kg-2E1H/h. Butanol recovery in the top was fixed to 0.99.

Table 5-2. Sensibility analysis in Aspen Plus using 2E1H-OAL as mixed extractant

Y	a	B	Regression
Pre-heated OAL[MJ/Kg-ABE]	0.289	2.402	Lineal
Cooled OAL [MJ/kg-ABE]	0.015	8E-02	Lineal
Boiler [MJ/Kg-ABE]	0.071	1.099	Lineal
Condenser (MJ/Kg-ABE)	0.020	0.651	Lineal
Diameter [m]*	0.149	0.232	Potential
Aux-condenser [MJ/(Kg-ABE]	0.051	0.880	Potential
LMTD preheater	74.72	-0.020	Potential
LMTD cond.	4.268	46.296	Logarithmic

Lineal (y=a+b*x)
Potential (y=a+x^b)
Logarithmic (aLn(x)+b)
x (kg-OAL/kg-ABE), *x(kg-OAL)

Concentrations of ABE performed with Matlab in optimal condition was compared with Aspen Plus® simulation to verify equilibrium model. In the Matlab® and Aspen Plus® simulation of acetone, ethanol and butanol concentration were 4.7, 1.7, 5.3 g/L and 4.4, 1.9 and 5.4, respectively. The reactors number and the sizing reactor were 8 and 994 m^3 in the optimization at a substrate cost of 0.12 $/kg, respectively. The butanol, ethanol and acetone yield in simulation were 0.23, 0.018 and 0.052 kg-solvent/kg-substrate, respectively.

The ABE productivity was 0.85 g/L/h. Productivity was 2.5 times higher than SFS in optimal conditions. TAC was 0.683 $/kg-ABE. Investment of hybrid reactor and extractant regeneration system was 23.8 MUSD. 60.4% of total investment was caused by the reactor cost. In ratio to SFS process investment save was of 38.2% mainly by reactor reduction cost. TAOC was 21.2 MUSD/year. Substrate and enzyme purchasing and steam production were 79.7%, 15.5% and 2.7% of TAOC without separation, respectively.

Enzymes supplementation were reduced in 50% and ABE yield was increasing of 0.29 to 0.3 g-ABE/g-substrate, in consequence TAOC of the hybrid reactor and extractant regeneration system was reduced in 5.4% in ratio to SFS. EP without separation was 10.9 MUSD/year. EP and TAC were 5 times higher and 20.6% lower than SFS (0.12$/kg-substrate), respectively. The recovery cost in ratio to SFS was studied in distillation system section

5.3.3. Optimization of integrated fermentation and detoxification system

Sensitivity analysis was performed to determinate sizing functions for economic optimization of SFS-E (Table 5-3). The VaN recovery in distillation column was fixed to 0.99. In the optimization results, TAC was increasing of 0.686 to 0.721 $/kg-ABE, an increasing of 7.6%. Extractant used (48.7 kg-Extractant/kg-butanol) was 1.07 times higher than SFS-Ms. The butanol distribution coefficient in the reaction system was 2.7 by co-products and low butanol concentration (4.6 g/L).

Table 5-3. Sensibility analysis in Aspen Plus using pure OAL as extractant (ABE flow=5000 Kg/h)

Y	a	B	Regression
Pre-heated OAL [MJ/kg-ABE]	0.479	0.769	Lineal
Cooled OAL [MJ/kg-ABE]	0.015	-8E-5	Lineal
Boiler [MJ/(kg-ABE+kg-Vanillin)]	0.099	0.645	Lineal
Condenser (MJ/kg-ABE)	0.055	-0.074	Lineal
Diameter [m·(Kg-ABE+Kg-inhibitors)/(Kg-ABE)]	0.726	0.444	Potential
Auxiliary condenser [MJ/(kg-ABE+kg-Vanillin)]	0.033	0.617	Potential
Auxiliary condenser 2 [MJ/(kg-ABE+kg-Vanillin)]	0.223	0.584	Potential
LMTD preheater	81.49	-0.187	Potential
LMTD condenser	118.7	-0.167	Potential

Lineal (y=a+bx), Potential (y=a+x^b), x [kg-OAL/kg-ABE]

The number of reactors was equal to SFS-E, 8, with a productivity 3.4% lower. The investment without ABE purification was 24.2 MUSD; a TAIC 2.1% higher than SFS-Ms. TAC and TAOC without ABE purification were 21.8 MUSD/year and 0.72; 2.8 and 5.4% higher than SFS-Ms, respectively. EP without final purification and without butyric sell was 8.9 MUSD/year, 20% lower than SFS-Ms. The butyric acid purification and its cost to sell was studied in the distillation system section.

The experimental productivity of conversion of phenolic compounds and furfural in the batch process is reported between 0.03 to 0.15 g/L/h [165]. VaN and FuOL supplementation were studied at productivities of VaN plus FuOL less than 0.165 g/L/h. Additionally, in integrated reactor will be expected that increasing its velocity of conversion because with integrated reactors with high loadings and without inhibitors is achieved a higher biomass concentration than the batch process [88,90,134,177].

The TAC effect of concentration of hydrolyzed inhibitors can be observed in the Figure 5-5. In optimal conditions, VaN and FuOL concentrations were less than 0.33 and 0.78 g/L, to feed concentration of hydrolyzed inhibitors less than 30 g/L, respectively. At this concentration of FuOL inhibition was not caused (see the kinetic model in supplementary info A-1). TAC variations to concentrations of hydrolyzed inhibitors lower than 9 g/L was less than 1%. However, reactors number was increasing of 8 to 11 and TAC was reduced of 0.72 $/kg-product to 0.788 $/kg-product (0.12 $/kg-substrate), with fed of 13.5 g/L of inhibitors recovery (VaN, FuOL, and acetic acid to 4.5 g/L each one), respectively. TAC with supplementation of 30 g/L of hydrolyzed inhibitors was equal to SFS with an inhibitors concentration 2.2 times lower. The kinetic model predicted a butyric yield increasing of 0.008 to 0.05 g/g-substrate with increasing inhibitors supplementation to optimal conditions.

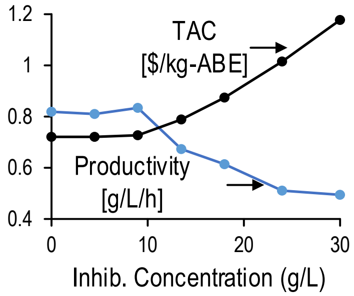

Figure 5-5. TAC and ABE productivity of hybrid system in optimal conditions to several hydrolyzed concentrations

5.3.4. Distillation system

TAC of thermally integrated distillation system by SFS, proposed in this work, was 0.12 $/kg-ABE. The energy requirements of separation from batch fermentation were 8 MJ-fuel/kg-ABE with ABE recovery of 0.975. 67% of unrecovered solvent was ethanol. The acetone unrecovered was found principally in non-condensable gas stream. While ethanol and butanol unrecovered were founded in vinasses. EP of SFS with separation was negative when substrate cost was higher than 0.1 $/kg.

Separation cost of SFS-Ms without regeneration extractant was 42% lower than SFS system. The energetic requirement of integrated distillation system without regeneration was 4.6 MJ-fuel/kg-ABE. However, including heat of regeneration boiler, the total energetic requirement was 12.5% higher than SFS system. TAC for total distillation system; and both reaction and separation systems were 0.163 and 0.747 $/kg, respectively. Extractant regeneration cost was 54% of TAC of distillation system. Separation cost of SFS-Ms was 26.4% higher than SFS system. However, TAC of SFS-Ms was 25.3% lower than SFS due to the high performance of the hybrid reactor. EP of SFS-Ms with purification was 7 MSUD/year.

In SFS-Ms, butyric acid was not recovery in distillation top.

Using pure OAL was recovered the 67% of total butyric acid produced (94 kg/h of butyric acid to 99.8% of purity). Acetic acid was consumed totally by the biocatalyst in all simulations to optimal conditions. The total energetic requirement of SFS-E and extractant regeneration were 9.5 and 5.1 MJ-fuel/kg-ABE, respectively. TAC of distillation system of SFS-Ms was 0.177, 8.6% higher than SFS-Ms. While, EP of SFS-E was 6.4 MUSD/year, 8.5% lower than SFS-Ms. Butyric acid sell was 1.5 MUSD/year. TAC was increased of 15.2 MUSD/year when substrate cost was reduced of 0.12 to 0.06 $/kg-substrate.

Has been reported energy consumption of 14 MJ/kg-ABE using solvent mixed, OAL-Decane, [66]. [89] reported energetic requirements of 8.7 MJ/kg-butanol, the extraction conditions are not specified in this report. Energetic requirement using OAL reported by [131] was 18.5 MJ/kg-butanol. Extraction to high-temperature than fermentative [131] and dual fermentative extraction [132] are the extraction systems with lowest energy requirement reported in the literature (between 3.8 and 4.6 MJ/kg-butanol). These are external systems, therefore, cannot better the performance of the reactor. However, equitable evaluation for a conclusion of extraction system with the less energetic requirement can be not realized because energetic integration and rigorously of simulation is different in all report.

The energetic requirement in biobutanol production with a recovery of hydrolyzed inhibitors has been not reported in the literature. In this work, energetic requirement with inhibitors supplementation of 4.5, 13.5, 18 and 30 g/L were 11, 15, 19 and 38 MJ-fuel/kg-ABE or 10.4, 12.3, 15.4 and 26.5 MJ/kg-products, respectively, when butyric acid, VaN and FuOL recovered were include as products. The energetic requirement was increased because extractant necessary increasing with inhibitors supplementation. Inhibitors supplementation lower than 13.5 g/L can be recommended from energetic point view because exponential behavior was observed from this point. The separation cost of the distillation system without regeneration and inhibitors supplementation was between 0.077 and 0.082 $/kg-ABE.

The EP of reaction and separation system will be not necessarily lowered with inhibitors supplementation because phenolic compounds and furans have a high cost of sell. For instance, the industrial cost of VaN and FuOL are 10.5 and 1.9 $/kg, respectively [138]. EP to several cost of sell minus its separation of hydrolyzed inhibitors can be observed in the Figure 5-6. The necessary cost for equal SFS-Ms performance was between 0 and 0.9 $/kg-inhibitors in the majority of evaluating cases. Interestingly, EP with 9 g-inhibitors/L supplementation into reactor was equal to SFS-Ms with a null cost of selling of hydrolyzed inhibitors. This result, EP higher than without inhibitors, was possible because the objective function was the TAC and not the EP, and yield of butyric acid was increased with inhibitors supplementation.

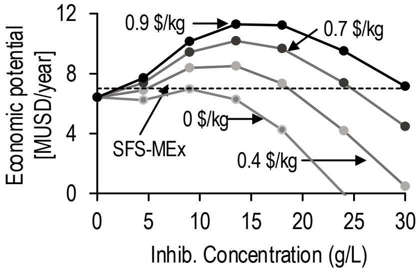

Figure 5-6. Economic potential of SFS-E to several concentrations of hydrolyzed inhibitors and sell costs of inhibitors minus its recovery cost ($/kg-inhibitor-recovery)

When optimization of SFS-E was realized with EP as the objective function, energetic requirement of regeneration and EP without inhibitors supplementation was 7.2 MUSD/kg-product and 7.8 MJ-fuel/Kg-product, respectively. An increasing with respect to TAC optimization of 12.5 and 48.3% for EP and energetic consumption of regeneration, respectively. Inhibitors cost of sell for equal SFS-Ms performance was between 0.75 and 1.7 and 0.3 and 1.56 $/kg-inhibitor when butyric acid sell was assumed zero and the butyric acid recovery was equal to without inhibitors supplementation. In all sceneries of inhibitors cost, sell cost was less than the actual cost of sale of FuOL. However, separations cost of inhibitors must be realized to determinate economic viability of the process.

5.4. Conclusions

The energetic requirements of SFS were lower by more than 11% with respect to extractive fermentation systems for heat integration of the distillation system. However, this process was not viable for its low productivity and high enzyme cost. Reactor and enzyme cost was reduced in more than two times using extractive fermentation; therefore, the process was profitable. The extractive fermentation was an effective way to reduce inhibition of hydrolyzed. However, the energetic requirement was increasing of 12.3 to 26.5 MJ-fuel/kg-product, when inhibitor supplementation was increasing of 13.5 to 30 g/L, respectively.

6. Dynamics and control of a hybrid reactor with liquid-liquid extraction by ABE production

Resumen

In this chapter was realized a dynamic study of ABE production in a reactor integrated with detoxification. The best operational conditions were selected by the minimization of the perturbations effect in the economic potential. The economic potential to optimal conditions of middle operation was reduced with perturbations in 13%. The similar way, the energetic requirement was increasing of 7.1 MJ/Kg-ABE to 7.3 MJ/kg-ABE, to perturbation between 20% and 30% by cellulose and hydrolyzed inhibitors. The economic potential was reduced only 4.7% in ratio to operation without perturbation without a control of concentrations into the reactor; energetic requirement of fermentation system by extractant regeneration was increasing to 8 MJ/kg-ABE.

Keywords: Multiplicities steady, TAC, optimization

6.1. Introducción

Industrial acetone, butanol and ethanol (ABE) production is realized by several clostridia. Lignocellulose is the most abundant substrate in the world for ABE production. However, butanol and hydrolyzed inhibitors are very toxic for biocatalyst and its production is not feasible in the conventional batch process. In an integrated reactor with pervaporation and vacuum evaporation, the butanol can be recovered. However, hydrolyzed inhibitors produced in the pretreatment, is not recovered economically in these systems due at its high-boiling point. These inhibitors can be recovered in a simultaneous fermentation-detoxification system with liquid-liquid extraction. Energetics requirement in optimal conditions is between 10 and 26.5 MJ-fuel/kg-product with supplementation of hydrolyzed inhibitors between 0 and 30 g/L, respectively.

The main limitation of any steady-state process design is its ability to handle uncertainties and disturbances occurring during the process operation that causes variability in plant performance[178]. These disturbances, affect the concentrations into the reactor and profitably of the process. For instance, if inhibitors feed into the reactor is increasing in continuous operation the performance of reactor can be drastically reduced. Therefore, a robust control can be necessary.

Conventionally the control is realized to have stable conditions of concentration or temperature into the reactor. For instance, Mariano et al.[64] studied an integrated reactor with vacuum evaporation for biobutanol production from glucose.

Control was difficult because vapor-liquid equilibrium was very sensitive a changes of substrate concentration and fermentation temperature. The fluctuations of substrate concentration, in this external integrated system, are controlled with the feed flow to the reactor and the feed flow to the evaporator. The objective of control is to keep substrate and/or butanol concentration in the fermentation constants. However, variations in this feed flow affect the economy of fermentation; for instance, decreasing the feed flow to reactor decreasing the product flow or increasing the feed flow to evaporator increasing the power requirement of the compression system.

In this chapter, a parametric sensitivity of the total annualized cost (TAC) was realized. Selection of optimal conditions and better strategy of control was performed.

6.2. Mathematical model

The fermentation time was fixed to 500 h, the reactor started in batch at a cellulose concentration of 20 gL^{-1}. The maximum volume of reactors was 1000 m^3. Oleyl alcohol was selected as the extractant in this work by its high-boiling point and biocompatibility. Efficiency in the reaction system was fixed to 0.8. The cost of sale of butanol assuming in this work were acetone, ethanol, OAL and butyric was 1, 0.7, 0.8, 2[138] and 4.3[138] \$/kg, respectively. The feedstock flow and its cost were 25000 kg-dry-lignocellulose/h and 0.08 \$/dry feedstock, respectively.

The feedstock cost was 1.4 times higher than corn stover[179]. The middle conditions supposed in this work was 120 and 13.5 g/L of cellulose and hydrolyzed inhibitors, respectively. Hydrolyzed inhibitors (acetic acid, Furfural, and phenolic compounds) were fed into the reactor to the same ratio (1/1/1) in all cases tested. VaN and furfural were used in the representation of furans and phenolic compounds, respectively (see chapter 5, thermodynamic properties).

The average ratio of cellulose/xylose/lignin was 1/0.5/0.7. In this work, substrate word was referred to the sum of cellulose and xylose. Balances of the reactor can be observed in supplementary info D. The optimization function was the economic potential of the reactor and regeneration system. Optimization variables were enzyme and extractant loading, dilution rate and time of start-up of bleeding, continuous feed, and butanol separation. Maximization was performed in Matlab using its optimization toolbox.

6.3. Result and analysiss

4.1.1 Steady state multiplicities of extractant regeneration system

A study of the behavior of the regeneration system was realized due to high nonideality of separation. The extractant loss in the top was fixed after observing steady-state multiplicity in the separation. The multiplicities obtained by 2,5-DMF can be observed in Figure 6-1. The multiplicity zone was achieved when less extractant loss was achieved in the top. The recovery of 2,5-DMF was reduced exponentially when the extractant loss in the top or condensation heat were reduced or increasing, respectively. A similar behavior was observed in VaN recovery. An extractant regeneration system with loss of extractant in the top was proposed to avoid these multiplicities (The extractant will be recovered as chapter 5). In the simulations was observed that losses in the top of OAL higher than 1000 kg-OAL/h were sufficient greatly for not operation in the multiplicity zone. For this reason, extractant loss in the top was fixed to 1000 kg/h. Extractant recovery of the top

OAL was studied in chapter 5.

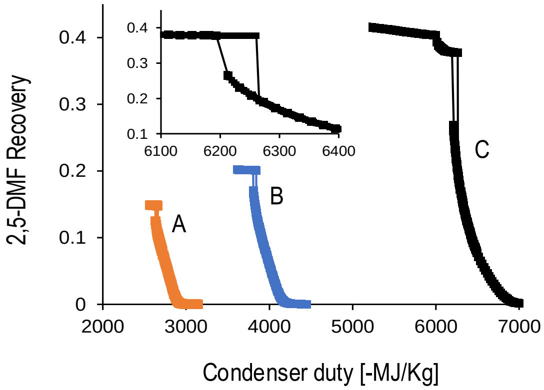

Figure 6-1. Steady-state multiplicity in extractant regeneration column to several recovery of 2,5-DMF. Boiler heat of C>B>A

4.1.2 Volume control of integrated reactor

Volume control of aqueous and the organic phase of the reaction was realized with an ideal proportional control. Proportional constant in both cases was 10. Variables of control were the purge of aqueous and the organic phase. The volume of the organic phase and aqueous phase can be measured using a modified decanter design [180]. The profiles of volume control can be observed in Figure 6-2. Profiles were developed with reactor conditions with perturbations described in the next section. Proportional constant in both cases was 10. Proportional control was the sufficiently rigorous by ideal conditions. However, in realistic conditions, for instance, noise or accuracy, can disturb the effectivity of control. Therefore, a control integral can be necessary

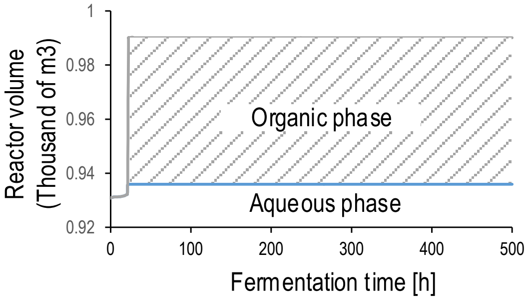

Figure 6-2. Reactor volume of the organic phase and aqueous phase.

Temperature and pH control were not studied because a kinetic model with its effects was not considerate. Rheology and mass transfer effects were not studied in this work. However, this effects can reduce the reactor performance. Alternatively, the mass transfer effect in the reaction for biobutanol production can be reduced in a multi-stage reaction system because several agitation conditions or temperatures can be performed in each reactor.

4.1.3 Sizing and operational conditions of reactor system

The sizing of the process affects the controllability because if the sizing is low for a non-appropriate response of control of profitability of reactor can be decreased drastically. Optimizations of TAC were realized to obtain the sizing of the reactor system and variables of operation to several conditions. The range of optimizations was performed at a changed maximum of 30% and 20% in hydrolyzed inhibitors and cellulose concentrations.

The cellulose conversion achieved in this work was around of 62 to 68%. In NREL reported is achieved a conversion of cellulose to glucose of 91.2% in a batch process without simultaneous fermentation[181]. However, an enzyme loading of 20 mg-protein/g-cellulose was needed. NREL need an enzyme load between 4 to 5 times higher than the obtained in this work (Figure 3). In other words, in this thesis the enzyme cost was higher than economic benefits to achieve conversions higher than 68% of cellulose.

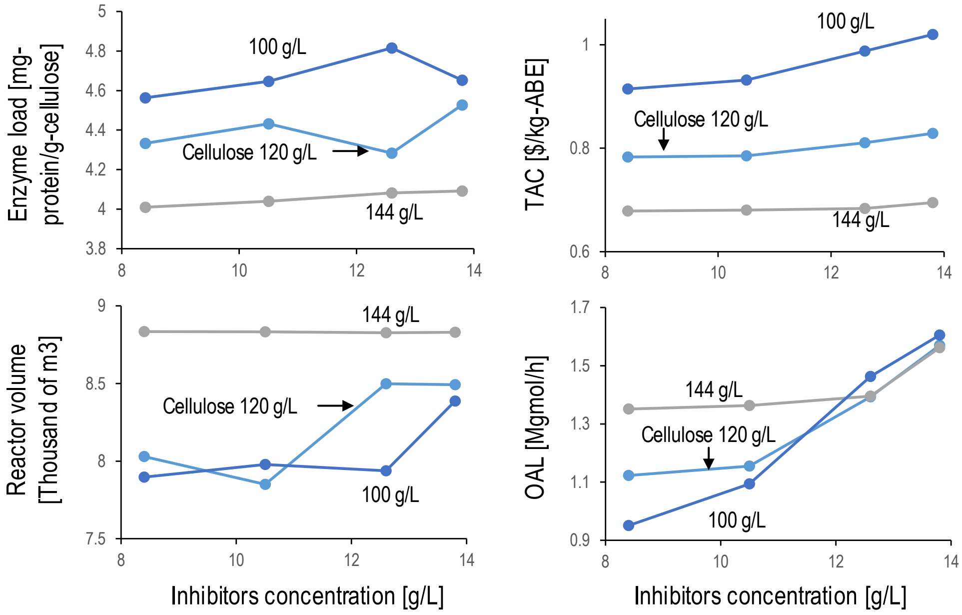

Figure 6-3. Optimal conditions to several hydrolyzed inhibitors and cellulose concentrations

The TAC and OAL flow were increasing with inhibitors concentration in all cases evaluated. In some cases of the optimization of the economic potential was preferred decreased the enzyme loading and increasing the reactor volume when the inhibitor was increasing. The TAC was reduced between 15 and 35% when the cellulose concentration was increasing in 20% because the feedstock had less structural carbohydrates. Low concentration of substrate needs less extractant due to the purge flow. The purge flow increasing because more water is fed to the reactor.

The variables that can be used in the control are the extractant flow, the feed flow, the enzymes flow, and water dilution. In the control with extractant flow is a necessary oversize extractant regeneration system, due to a close-up loop of extraction is necessary more initial investment of extractant. Control with the feedstock is limited by substrate stock and reduce feedstock reduce the product flow. Enzymes can be an interesting variable of optimization; however, the low sensibility to economic potential in ratio to enzyme flow makes of this an insufficient option. In this work, minimization was proposed for avoiding or to minimize the effect of perturbations.

The optimization with perturbations was performed at 10 random functions less than 30% of cellulose. Hydrolyzed inhibitors variations were 1.5 higher than cellulose concentration. The aleatory functions were founded before the fermentation using the function "rand" of Matlab® (Aleatory-function = (rand-rand)*0.3 for the cellulose change). The aleatory function had 10 perturbations. The perturbations were realized each 36 hours after of 136 h of beginning the fermentation.

The objective function of optimization was the mean economic potential. After optimization, random functions was increasing to 30. The mean economic potential using the design conditions found without perturbations was reduced of 8.6 to 7.5 MUSD/year; mean energetic requirement was increasing of 7.1 to 7.3. The maximum reduction was 2.4 MUSD/year. While, in the optimization with perturbations was 8.2 MUSD/year, and mean energetic requirement was increasing of 7.1 to 8 MJ/kg-ABE. The maximum reduction in ratio to optimal conditions without perturbations was 1.1 MUSD/year, a reduction 54% less. This diminution was achieved because the variation of cellulose concentration into the reactor was lower (see an example of a aleatory perturbation function, in Figure 6.4). However, the energetic requirement was increasing because in the optimization with perturbations the extractant needed was 8% higher.

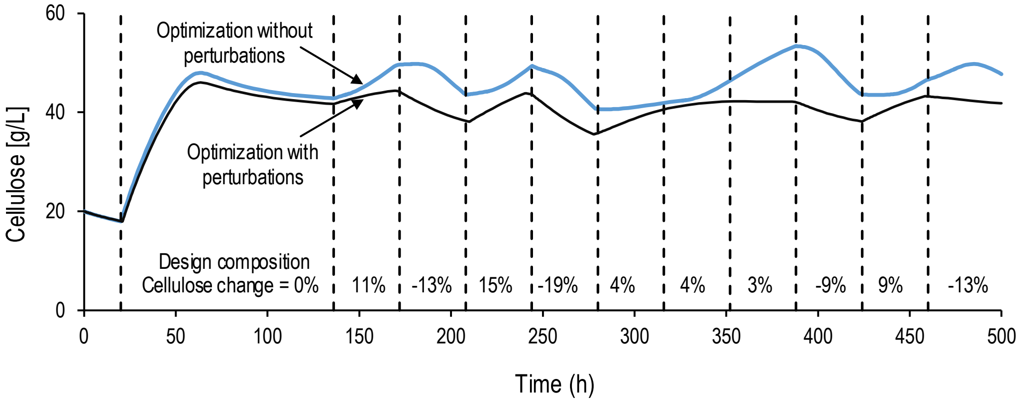

Figure 6-4. Optimal conditions to several hydrolyzed inhibitors and cellulose concentrations

6.4. Conclusiones

In this chapter was proposed a strategy of optimization than reduce the negative effect of perturbations in the performance of reactor system. A proportional control was the sufficiently robust by ideal control of reactor volume. A loss flow of OAL higher than 1000 Kg/h in the top was necessary to avoid multiplicities. The process was stable with perturbations each 36 hours. In evaluation with perturbations, with an optimization in without perturbations was achieved an economic potential 1.3 MUSD/year lower than optimization with perturbations. However, energy requirement was increasing in 0.7 MJ/kg-ABE.

7. Conclusions and future work

7.1. Conclusions

- The energetic requirement of distillation systems studied in this work was the lowest requirement by distillation reported until the date by ethanol, isobutanol, and ABE recovery.
- The thermally integrated distillation systems proposed in this work with vapor compression and double-effect distillation allow to decrease the fuel requirement of distillation systems without recovery of condensation heat, between 50-70% and 30-40%, respectively.
- Double effect distillation was the most economical way by ethanol, isobutanol or ABE recovery from external systems due to the high compressor and electricity cost in vapor compression distillation.
- The energetic requirement of external extraction systems, high-temperature extraction, and dual extraction were the less economical and energetically attractive options than distillation systems studied in this work.
- Mixed extraction and extractant regeneration with direct steam distillation with end purification by double-effect distillation system were options with energetic requirement lower than double-effect distillation without extraction.
- Vapor compression distillation proposed in this thesis was the recovery integrated system with the lowest fuel requirement.
- Direct steam distillation proposed in this work was the most economical option by extractants with a high-boiling point, because allowed using low-pressure steam, reduced the exchanger area of regeneration and increasing energetic integration. However, is not recommended when the substrate having inhibitors hydrolyzed.
- Integrated reactor with vacuum evaporation was an option less attractive energetically than double-effect distillation system. However, was an option more economical than reaction system without integrated recovery, because was improve the reactor productivity.
- A heat pump was an efficient way for heat recovery in flash evaporation due to CO_2 compression.
- TAC and energy requirements of the PTMSP-ceramic membrane were between 1 to 7.5% higher and 11 to 28% lower than integrated reactor with vacuum evaporation. However, the stability of PTMSP membranes is lower than PDMS membranes, and this effect not studied in this work.

- High selective membrane, TOA, not was a better choice than continuous fermentation process without simultaneous recovery by its low permeability.
- An effective detoxification method must be used if SFS-E or SFS-P is applied in industrial scale for butanol manufacture from lignocellulose.
- The extractive fermentation with oleyl alcohol was an effective way to reduce inhibition of hydrolyzed. However, the energetic requirement was increasing when inhibitor supplementation was increasing of 13.5 to 30 g/L of 12.3 to 26.5 MJ-fuel/kg-product, respectively.
- Optimization of process with perturbations is an effective way of reduce the impact of distubations.

7.2. Future work

In this thesis was evaluated the performance of several integrated reactor systems, however, several questions have been not resolved yet. One of them is the agitation velocity than must be used in extractive fermentation with oleyl alcohol. For instance, enzymatic hydrolysis can need different agitation velocity than extraction or fermentation. However, multiple reactors in series with recirculation can be used to carry out the process and decreasing the rheological and mass transfer effect in the reactor system.

The effect of operational temperature in the performance of the reaction system was not studied in this thesis. However, the temperature is an important parameter of the process. Developed of a kinetic model for fermentation with temperature effect is recommended. Of similar way, multiple reactor systems can be performed and several operational parameter can be optimized to improve the reactor performance. Nutrients supplementation into the reactor was not studied in this work. However, it is expected than low nutrient supplementation will be needed by a high-loading operation. Integration of ethanol and butanol production in 2G plant study is necessary by optimization of the process because heat integration play a role important in profitably of process.

Supplementary info A: Thermodynamic model

Activity was calculated from UNIQUAC [182]. The binary parameters for liquid-vapor equilibrium can be observed in the Table 1 and structural paraters were: acetone, R=2.57 and Q=3.34; 1-butanol, R=3.9243 and Q=3.668; water, R=0.92 and Q=1.4; isobutanol, R=3.543 and Q=3.048; etanol 2.1055 and Q=1.972.

Table A-1. Binary parameters of UNIQUAC model by liquid-vapor equilibrium

	Butanol (1) –water(2)	Isobutanol(1)-water(2)	Acetone(1)-water(2)	Ethanol(1)- water(2)
a_{12}	155.31	150.949	14.865	123.9261
a_{21}	-579.36	142.459	97.472	-226.2537
b_{12}	1.0822	0	-0.019	-0.5395
b_{21}	2.5715	0	0.963	1.1212
c_{12}	-43.711e-4	0	0	4.94e-4
c_{21}	-6.77e-4	0	0	-0.0011
d_{12}				
d_{21}				
Reference	[183]	Aspen plus	Aspen Plus	Aspen plus

Donde $G_{ij} = \exp(-(A_{ij} + B_{ij}T + C_{ij}T^2)/T)$

Parameters adjusted in this work by terniary equilibriums 2E1H-water-solvent can be observed in the Table A-2.

Table A-2. UNIQUAC temperature dependent binary parameters for liquid-liquid extraction using 2E1H

Component i Component j	Butanol 2E1H	Agua 2E1H	Acetone 2E1H	Ethanol 2E1H	Butanol Agua
Source	This work	This work	This work	This work	Aspen LL
Aij	-0.581	-2.676	0.040	0.403	-70.97
Aji	-0.327	-1.510	0.240	-0.517	6.63
Bij	-107.05	364.29	221.44	111.13	3132.83
Bji	258.21	239.91	-782.69	-514.59	-16.49
Cij	-	-	-	-	10.63
Cji	-	-	-	-	-1.32
Tlower	298.20	298.20	298.20	298.20	308.15
Tupper	313.20	313.20	313.20	313.20	396.45

UNIQUAC binary parameters were adjusted to dodecanol-ethanol-water experimental equilibrium because this equilibrium non can be desbribed by UNIFAC (Figure A-2).

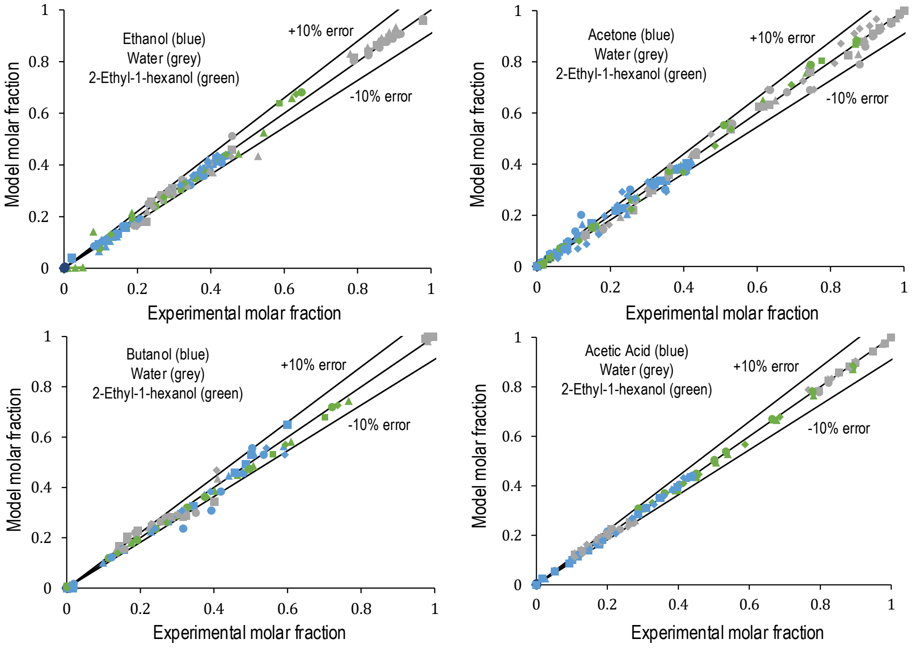

Figure A-1. Parity diagram of 2E1H-water ternaty liquid-liquid equilibrium with acetone, butanol, acetic acid and ethanol Parity diagram for 2E1H-water-solvent can be observed in the Figure A-1

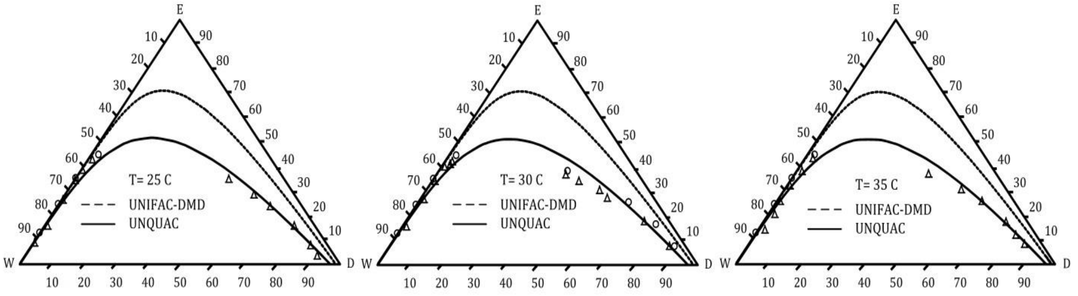

Figure A-2. Ternary diagram by ethanol-dodecanol-water equilibrium. (%) mass. Experimental data reported by Boluda et al.[184], △, and Kirbaslar and Cehreli [185] ,○.

Supplementary info B: Cost function

The total investment cost of the process (TIAC) in the optimization was given by:

$$TIAC = C_R + C_T + C_{IN} + C_{COMP} + C_M \cdot t_m + C_{EI} \tag{B-1}$$

Columns cost, C_T, heat exchange, condenser and reboiler costs, C_{IN}; and compressors costs, C_{COMP}, were calculated with functions of installed cost report by Douglas [114]. Reactor cost, C_R, was calculated from function reported by Oudshoorn et al. [79]. C_{EI}, was the initial inversion of extractant. Functions cost can be observed in Table B-1. The fabrication material selected was stainless steel. It is assumed that the lifetime of the membranes is 3 times lower than other equipment, in consequence t_m ratio is equal to 3. The membrane cost (C_M) was given by:

$$C_M = A_M \cdot C_{AM} \tag{B-2}$$

Table B-1. Functions by equipment installation

Equipment	Purchase function	Installation factor	Equation
Reactor	$(\$) = 4123 \cdot V_R^{0.608} + 22530$ (year 2010)	4.93	(B-4)
Tower (MOC:SS)	$(\$) = \left(\frac{M\&S}{280}\right) \cdot 101.9 \cdot D_c^{1.06} \cdot L_c^{0,802}$	5.85	(B-5)
Trays (Type: Sieve; MOC:SS)	$(\$) = \left(\frac{M\&S}{280}\right) \cdot 4.7 \cdot D_c^{1.06} \cdot L_c$	4.5	(B-6)
Exchanger heat and boilers	$(\$) = \left(\frac{M\&S}{280}\right) \cdot 101.3 \cdot A^{0.65}$	7.3	(B-7)
Condenser	$(\$) = \left(\frac{M\&S}{280}\right) \cdot 101.3 \cdot A^{0.65}$	6.04	(B-8)
Compressor	$(\$) = \left(\frac{M\&S}{280}\right) \cdot 517.5 \cdot bhp^{0,82}$	3.1	(B-9)

D_c and L_c were the diameter and the high of column (ft),A_c is the exchanger area (ft^2) and bhp is the compressor work (bhp), $M\&S$ was marshal and Swift index, V_R was the reactor volume (m^3)

Where A_M, is the membrane area and C_{AM} is the total installed membrane cost (\$/m^2). Total operational annualized cost, *O* (\$):

$$TOAC = C_E + C_V + C_{AE} + C_S + C_{Ez} + C_{EX} \tag{B-3}$$

Where: C_E, C_V, C_{AE}, C_S, C_{Ez}, C_{EX} are annualized costs of electricity, steam, cooling water, substrate, enzymes, extractant loss, respectively.

Supplementary info C: Kinetic model

Experimental data of fermentations were reported by Shinto et al. [152] and Shinto et al. [151] Parameters were adjusted to 8 experimental fermentations, 4 for each substrate (glucose and xylose). Biocatalyst was *C. saccharoperbutylacetonicum* N1-4. Phenolic compounds and furans experimental effect was reported by for *C. saccharoperbutylacetonicum* N1-4 to same temperature and pH than glucose and xylose fermentations. However, not nutrient supplementation was performed. The kinetic model for prediction of glucose and xylose consumption without hydrolyzed inhibitors, had 12 parameters lower than model proposed by Shinto et al. [151]. The kinetic model was described by the next equations:

$$r_1 = \frac{V_{\max 1}[\mathrm{Glucose}][\mathrm{Biomass}]}{Km_1 + Glucose + Km_1 \cdot \left(\frac{[Glucose]}{Km_{a1}}\right)^2} \cdot F \cdot I_b \tag{C-1}$$

$$r_2 = \frac{V_{\max 2}[\mathrm{Piruvate}][\mathrm{Biomass}]}{Km_2 + [\mathrm{Piruvate}]} \cdot F \tag{C-2}$$

$$r_3 = \frac{V_{\max 3}[Acetate][\mathrm{Biomass}]}{Km_3 + [\mathrm{Acetate}]} \cdot F \tag{C-3}$$

$$r_4 = \frac{V_{\max 4}[Biomass]}{\left(Km_{4a} + [Acetate]\right)\left(Km_{4b} + [ACoA]\right)} \tag{C-4}$$

$$r_5 = \frac{V_{\max 5}[ACoA][\mathrm{Biomass}]}{Km_5 + [ACoA]} \cdot F \tag{C-5}$$

$$r_6 = \frac{V_{\max 6}[ACoA][\mathrm{Biomass}]}{Km_6 + [ACoA]} \cdot F \tag{C-6}$$

$$r_7 = \frac{V_{\max 7}[ACoA][\mathrm{Biomass}]}{Km_7 + [ACoA]} \cdot F \tag{C-7}$$

$$r_8 = \frac{V_{\max 8}[Glucose][Biomass]}{Km_8 + Km_{a8}/[BCoA] + [Glucose]} \cdot I_{NB} \cdot I_{NH} \tag{C-8}$$

$$r_9 = V_{\max 9} \cdot Biomass \cdot r_{g/x} \tag{C-9}$$

$$r_{10} = \frac{V_{\max 10}[ACoA][\mathrm{Biomass}]}{Km_{10} + [ACoA]} \cdot F \tag{C-10}$$

$$r_{11} = \frac{V_{\max 11}[Biomass][\mathrm{B}utyrate][\mathrm{AACoA}]}{([\mathrm{AACoA}] + \mathrm{Km}_{\mathrm{11a}})([\mathrm{Butyrate}] + \mathrm{Km}_{\mathrm{11b}})} \tag{C-11}$$

$$r_{12} = \frac{V_{\max 12}\left[Butyrate\right]\left[Biomass\right]}{Km_{12} + \left[Butyrate\right] + {Km_{a12}}/{\left[Butyrate\right]} + {Km_{b12}}/{\left[Bu\tan ol\right]}} \cdot F \tag{C-12}$$

$$r_{13} = \frac{V_{\max 13}[\mathrm{B}CoA][\mathrm{Biomass}]}{Km_{13} + [\mathrm{B}CoA]} \cdot F \tag{C-13}$$

$$r_{14} = \frac{V_{\max 14}\left[BCoA\right]\left[Biomass\right]}{Km_{14}\left(1 + Km_{a14}/\left[Butyrate\right]\right) + BCoA\left(1 + \left[Bu\tan ol\right]/Km_{b14}\right)} \cdot F \tag{C-14}$$

$$r_{15} = \frac{V_{\max 15}\left[Xylose\right]\left[Biomass\right]}{Km_{15}\left(1 + \left(\frac{[Xylose]}{Km_{15b}}\right)^2\right) + [Xylose]} \cdot (1 - r_{g/x}) \cdot \mathrm{I}_{\mathrm{NB}} \cdot F \tag{C-15}$$

$$r_{16} = \frac{V_{\max 16}\left[Xylose\right]}{Km_{16} + [Xylose] + {Km_{16a}}/{[\mathrm{BCoA}]}} \cdot \mathrm{I}_{\mathrm{NB}} \cdot \mathrm{I}_{\mathrm{NH}} \cdot F \tag{C-16}$$

$$r_{17} = V_{\max 17}\left[Biomass\right] \cdot (1 - \mathrm{r}_{\mathrm{g/x}}) \tag{C-17}$$

$$I_{NB} = \left(1 - \frac{\left[Bu\tan ol\right]}{\left[Bu\max\right]}\right) \tag{C-18}$$

$$I_{NH} = \left(1 - \frac{[Phenolic]}{[\mathrm{Phemax}]}\right)\left(1 - \frac{[Furans]}{[\mathrm{Furmax}]}\right)^{n_F}\left(1 - \frac{[Acetate]}{[\mathrm{Acemax}]}\right)\left(1 - \frac{[Butyrate]}{[\mathrm{Butmax}]}\right)\left(1 - \frac{[Biomass]}{[\mathrm{Bimax}]}\right)\left(1 - \frac{[Acetone]}{[\mathrm{Acemax}]}\right) \cdot \left(1 - \frac{[Glu\cos e]}{[\mathrm{Glumax}]}\right)\left(1 - \frac{[Xylose]}{[\mathrm{Xymax}]}\right) \tag{C-19}$$

$$r_{g/x} = \left(\frac{\left[Glu\cos e\right]}{\left[Xylose\right]}\right) \tag{C--20}$$

Global reaction, R [mmol/h], (Figure C-1) by component without hydrolysis were described by the following equations:

$$R_{Glu\cos e} = -r_1 \tag{A-19}$$

$$R_{Pyruvate} = -r_6 + r_1 + r_{15} \tag{A-20}$$

$$R_{ACoA} = r_2 + r_3 + r_4 - r_5 - r_6 - r_7 \tag{A-21}$$

$$R_{AACoA} = r_6 - r_4 - r_{10} - r_{11} \tag{A-22}$$

$$R_{Biomass} = r_8 + r_{16} - r_9 - r_{19} \tag{A-23}$$

$$R_{Acetate} = r_5 - r_4 - r_3 \tag{A-24}$$

$$R_{E\,\mathrm{thanol}} = r_7 \tag{A-25}$$

$$R_{BCoA} = r_{10} + r_{11} + r_{12} - r_{13} - r_{14} - r_8 - r_{16} \tag{A-26}$$

$$R_{Butyrate} = r_{13} - r_{11} - r_{12} \tag{A-27}$$

$$R_{Acetone} = r_9 + r_6 \tag{A-28}$$

$$R_{Bu\tan ol} = r_{14} \tag{A-29}$$

$$R_{Xylose} = -r_{15} \tag{A-30}$$

$$R_{Hydrogen} = -r_{20} \tag{C-31}$$

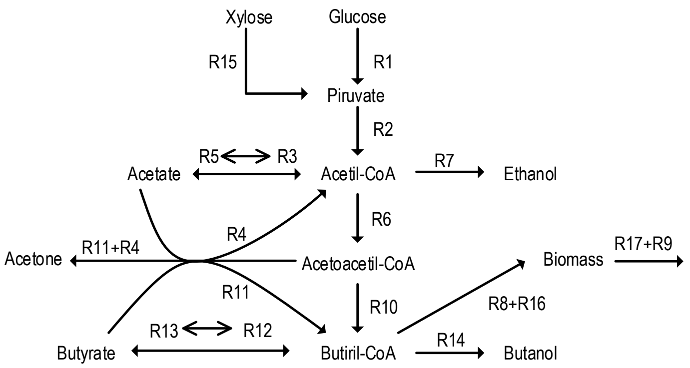

Figure C-1. Metabolic via of *C. acetobutylicum* using glucose and xylose as substrate

Parameters of model were adjusted with fminsearch function from Matlab software ®. Parameter minimization was realized in two stages: First, parameters were adjusted for error minimization in prediction of acetone, glucose, butanol, xylose, biomass, butyric acid and acetic acid concentrations reported Shinto et al. and Shinto et al. In the second stage, only 4 parameters additional were adjusted to simulate hydrolyzed inhibitors effect and parameters adjusted in first stage to experimental data reported was not changed. Vmax, Km, Kma and Kmb parameters of kinetic model found in this work can be observed in the Table C-1. Inhibition parameters of growth [Bumax], [Phemax], [Fumax], [Acmax], [Butmax], [Bimax], [Acemax], [Glumax] and [Xymax] were 212, 30.2, 42.7, 146.2, 342, 120.5, 1940 and 1830 mM, respectively; n_F was 0 if [Fumax] was less than 0.85 g/L or 3.4 if was higger.

Table C-1. Kinetic parameters of model development in this work

Rxn	Vmax	Km	Kma	Kmb
r_1	1.2	0.09	54.3	
r_2	27	22		
r_3	1.1	170		
r_4	156		312	17
r_5	2.7	16.1		
r_6	6.9	0.004		
r_7	144	1.0		
r_8	0.68	71.9		0.13
r_9	0.042			
r_{10}	79.1	8.0		
r_{11}	0.19	0.081	0.0027	
r_{12}	59.3	1.0	290	1070
r_{13}	12.7	2.11		
r_{14}	268	2.6	562	5.4
r_{15}	2.4	0.14	175.4	
r_{16}	0.13	62.5	0.96	
r_{17}	0.0072			

CO_2 and H_2 velocity reactions were obtained assuming stoichiometric production with respect to ideal reaction of acetone, butanol and ethanol. Correlation coefficient of glucose, acetone, butanol, xylose, acetate, butyrate and biomass were 0.987, 0.958, 0.985, 0.96, 0.888, 0.879 and 0.902, respectively. The profiles of the main metabolites for glucose and xylose fermentations can be observed in Figure C-2 and C-3, respectively

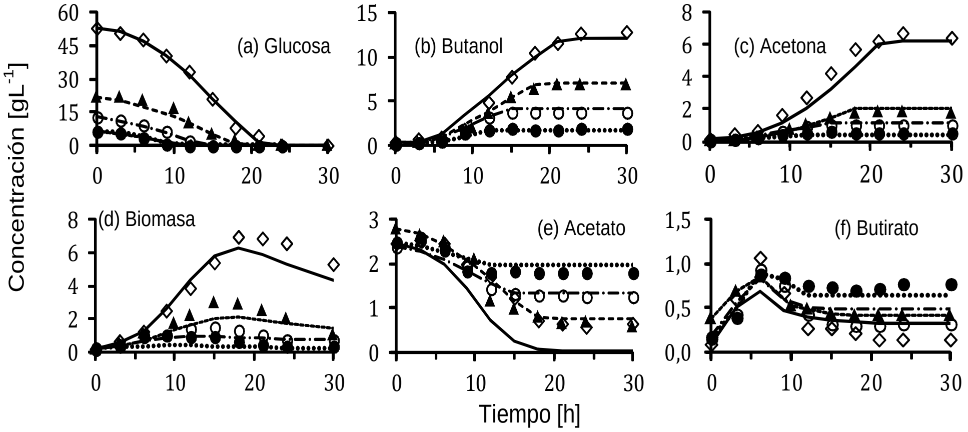

Figure C-2. Simulation perfil of kinetic model and its experimental data. Substrate glucose. Simulation: F5 (-), F6 (---), F7 (-··-), F8 (···). Experimental data: F5 ◆ , F6 ▲ , F7 ■, F8

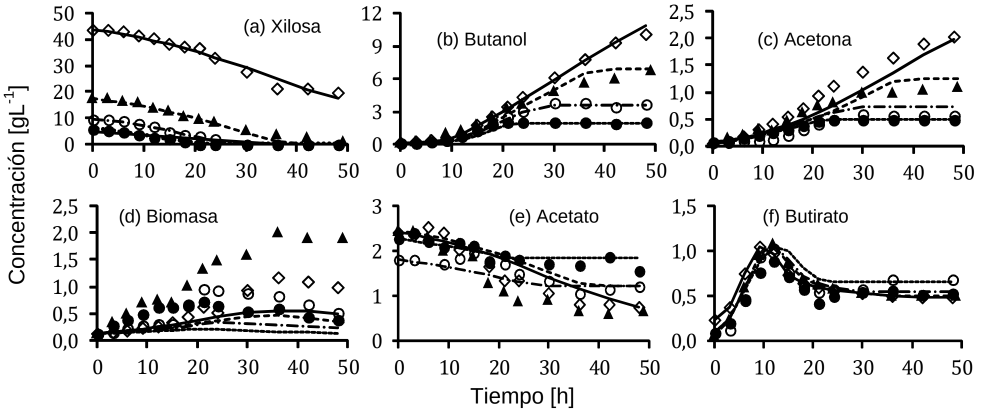

Figure C-3. Simulation perfil of kinetic model and its experimental data. Substrate xylose. Simulation: F5 (-), F6 (---), F7 (-··-), F8 (···). Experimental data: F5 ◆ , F6 ▲ , F7 ■, F8 ◇

Supplementary info D: Reactor model

Solids were assumed as void fraction in fermentation volume calculation. Overall reaction rate (R) of saccharification was obtained dividing the reaction rate of model proposed by Kadam et al. [154] for fermentation volume. Enzyme reactivity parameter is given by:

$$R_E = \frac{S(t)\cdot V(\mathrm{t}) + \int_o^{tf} x_{3s}\cdot F_3 \cdot dt}{x_{1s}\cdot F_1 \cdot (\mathrm{t_f}-\mathrm{t_a}) + \mathrm{S(0)}\cdot \mathrm{V(0)}} \tag{D-1}$$

Where: F_1 was feed flow, F_3 bleeding flow, x_s substrate mass fraction, *S* (g/L) cellulose concentration in the reactor at time (t), V total volume (L) at time t, the subindex *s* indicated lignocellulose, t_a and t_f were the times at which continuous fed begin and end fermentation respectively. fermentation volume V_F total volume (V_T).

General balance of integration reactor was:

$$\frac{dNi}{dt}_E = R_i \cdot V_F + F_1 \cdot x_{1i} - F_P \cdot x_{Pi} - F_G \cdot x_{Gi} + F_L \cdot x_{Li} - F_{Mi} \tag{D-2}$$

The simulation of simultaneous, fermentation, saccharification and liquid-liquid equilibrium were performed in pseudostady state (the reactor in transient state and the equilibrium unity in steady state). F_L is the aqueous phase obtained in decanter. Feed flow of aqueous phase (F_2) in the decanter if given by:

$$r_F = \frac{F_2}{F_{p1}} \tag{D-3}$$

Purge flow was obtained from a proportional controller of total volume. Gas flow (F_G) was calculated using proportional controller of pressure in reactor. F_2 is calculated fixed recycle ratio of fermentation (r_F). An integrated reactor with 99.95% efficiency of liquid-liquid extraction can be obtained if r_F is assuming as 0.9999. In this work, F_2 was calculated assuming a recycle of 0.95. The permeability of volatile compound i, was assumed equal for all components except butanol. The membrane selectivity (S_{bi}) is the ratio of butanol and i compound permeability:

$$S_{ib} = \frac{Per_i}{Per_b} \tag{D-4}$$

$$y_i \cdot P = x_i \cdot \alpha_i \cdot P_{sat} / \varphi_i \tag{D-5}$$

Activity coefficient, α, was calculated using UNIQUAC.

. In fermentative extraction, the liquid-liquid equilibrium was given by:

$$x_{I_i} \cdot \alpha_{I_i} = x_{II_i} \cdot \alpha_{II_i} \tag{D-6}$$

Pressure and vapor fraction in reactor was estimated with bubble pressure algorithm [186]:

$$y_i \cdot P = x_i \cdot \alpha_i \cdot P_{sat} / \varphi_i \tag{D-7}$$

Activity coefficient, α, was calculated using UNIQUAC. The fugacity coefficient in the vapor phase was calculated using the Peng–Robinson equation state. In Matlab® simulations, Henry's constant of H_2 and CO_2 in fermentation broth was assuming to be equal to the non-condensable in water.

The work of compressor, W, was calculated from:

$$W \cdot \eta_s = \frac{k}{k-1} \cdot z \cdot R \cdot T_1 \cdot \left[\left(\frac{P_2}{P_1} \right)^{\frac{k-1}{k}} - 1 \right] \tag{D-8}$$

In pervaporation, flux membrane, F_{Mi}, was given by [162]:

$$F_{Mi} = \int_0^{A_M} Per_i \cdot \left(x_i \cdot \gamma_i \cdot Psat_i - y_i P \right) dA \tag{D-9}$$

Where: $Peri$, γ_i, x_i $Psati$, y_i, P are the permeability [$gmolh^{-1}bar^{-1}m^{-2}$], the activity coefficient, the molar fraction in the reactor, vapor pressure [bar], the permeate fraction and vacuum pressure, respectively. The permeability of volatile compound i, was assumed equal for all components except butanol. The minimization was performed with optimization toolbox of Matlab®.

Bibliography

1. Lee, S. Y. *et al.* Fermentative butanol production by Clostridia. *Biotechnol. Bioeng.* **101,** 209–28 (2008).
2. Dürre, P. Biobutanol: an attractive biofuel. *Biotechnol. J.* **2,** 1525–34 (2007).
3. Cascone, R. Biobutanol - a replacement for bioethanol? *Chem Eng Prog* 104:S4-S8. (2008).
4. Jones, D. & Woods, D. Acetone-Butanol Fermentation Revisited. *Microbiol. Mol. Biol. Rev.* **50,** 484–524 (1986).
5. Green, E. M. Fermentative production of butanol—the industrial perspective. *Curr. Opin. Biotechnol.* **22,** 337–343 (2011).
6. Zverlov, V. V, Berezina, O., Velikodvorskaya, G. A. & Schwarz, W. H. Bacterial acetone and butanol production by industrial fermentation in the Soviet Union: use of hydrolyzed agricultural waste for biorefinery. *Appl. Microbiol. Biotechnol.* **71,** 587–97 (2006).
7. Tashiro, Y. & Sonomoto, K. Advances in butanol production by clostridia. *…, Technol. Educ. Top. Appl. …* 1383–1394 (2010).
8. Baez, A., Cho, K.-M. & Liao, J. C. High-flux isobutanol production using engineered Escherichia coli: a bioreactor study with in situ product removal. *Appl. Microbiol. Biotechnol.* **90,** 1681–90 (2011).
9. Shen, C. R. *et al.* Driving forces enable high-titer anaerobic 1-butanol synthesis in Escherichia coli. *Appl. Environ. Microbiol.* **77,** 2905–15 (2011).
10. Reyes, L. H., Almario, M. P. & Kao, K. C. Genomic library screens for genes involved in n-butanol tolerance in Escherichia coli. *PLoS One* **6,** e17678 (2011).
11. Inui, M., Suda, M. & Kimura, S. Expression of Clostridium acetobutylicum butanol synthetic genes in Escherichia coli. *Appl. Microbiol.* **8052,** 1305–1316 (2008).
12. Winkler, J., Rehmann, M. & Kao, K. C. Novel Escherichia coli hybrids with enhanced butanol tolerance. *Biotechnol. Lett.* (2010). doi:10.1007/s10529-010-0247-3
13. Atsumi, S. *et al.* Metabolic engineering of Escherichia coli for 1-butanol production. *Metab. Eng.* **10,** 305–11 (2008).
14. Rühl, J., Schmid, A. & Blank, L. M. Selected Pseudomonas putida strains able to grow in the presence of high butanol concentrations. *Appl. Environ. Microbiol.* **75,** 4653–6 (2009).
15. Nielsen, D. R. *et al.* Engineering alternative butanol production platforms in heterologous bacteria. *Metab. Eng.* **11,** 262–73 (2009).
16. Kataoka, N., Tajima, T., Kato, J., Rachadech, W. & Vangnai, A. S. Development of butanol-tolerant Bacillus subtilis strain GRSW2-B1 as a potential bioproduction host. *AMB Express* **1,** 10 (2011).
17. Winkler, J. & Kao, K. C. Transcriptional Analysis of Lactobacillus brevis to N-Butanol and Ferulic Acid Stress Responses. *PLoS One* **6,** e21438 (2011).
18. Berezina, O. V *et al.* Reconstructing the clostridial n-butanol metabolic pathway in Lactobacillus brevis. *Appl. Microbiol. Biotechnol.* **87,** 635–46 (2010).
19. Steen, E. J. *et al.* Metabolic engineering of Saccharomyces cerevisiae for the production of n-butanol. *Microb. Cell Fact.* **7,** 36 (2008).
20. Knoshaug, E. P. & Zhang, M. Butanol tolerance in a selection of microorganisms. *Appl. Biochem. Biotechnol.* **153,** 13–20 (2009).
21. Phillips, J. A. & Humphrey, A. E. in *In Wood and agricultural residues: research on use for feed, fuels and chemicals* (1983).
22. Butamax. *California Biobutanol Multimedia Evaluation. http://www.arb.ca.gov/fuels/multimedia/020910biobutanoltierI.pdf.* (2010).
23. Claassen, P. A. M., Budde, M. A. W., López-Contreras, A. M., Claassen, Â. P. A. M. & Lo, A. M. Utilisation of saccharides in extruded domestic organic waste by Clostridium acetobutylicum ATCC 824 for production of acetone , butanol and ethanol. **54,** 162–167 (2000).

24. López-contreras, A. M., Claassen, P. A. M., Budde, M. A. W. & López-contreras, A. M. Acetone , Butanol and Ethanol Production from Domestic Organic Waste by Solventogenic Clostridia. *J. Mol. Microbiol. Biotechnol.* **2,** 39–44 (2000).
25. Voget, C. E., Mignone, C. F. & Ertola, R. J. Butanol production from apple pomance. *Biotechnol. Lett* **7,** 43–46 (1985).
26. Marchal, R., Ropars, M. & Vandescasteele, J. P. CONVERSION INTO ACETONE AND BUTANOL OF LIGNOCELLULOSIC SUBSTRATES PRETREATED BY STEAM EXPLOSION. *Biotechno!ogy Lett.* **8,** 365–370 (1986).
27. Ezeji, T., Qureshi, N. & Blaschek, H. Production of acetone–butanol–ethanol (ABE) in a continuous flow bioreactor using degermed corn and Clostridium beijerinckii. *Process Biochem.* **42,** 34–39 (2007).
28. Qureshi, N., Saha, B. C., Dien, B., Hector, R. E. & Cotta, M. a. Production of butanol (a biofuel) from agricultural residues: Part I - Use of barley straw hydrolysate. *Biomass and Bioenergy* **34,** 559–565 (2010).
29. Jesse, T. W., Ezeji, T. C., Qureshi, N. & Blaschek, H. P. Production of butanol from starch-based waste packing peanuts and agricultural waste. *J. Ind. Microbiol. Biotechnol.* **29,** 117–123 (2002).
30. Gutierrez, N. A., Maddoxt, S., Schuster, K. C., Swoboda, H. & Gapes, J. R. Strain comparison and medium preparation for the acetone-butanol-ethanol (ABE) fermentation process using a substrate of potato. *Bioresour. Technol.* **66,** 263–265 (1998).
31. Ezeji, T. & Blaschek, H. P. Fermentation of dried distillers' grains and solubles(DDGS) hydrolysates to solvents and value-added products bysolventogenic clostridia. *Bioresour. Technol.* 5232–5242. (2008).
32. Parekh, S. Ethanol and butanol production by fermentation of enzymatically saccharified SO2-prehydrolysed lignocellulosics. *Enzyme Microb. Technol.* **10,** 660–668 (1988).
33. Wang, L. & Chen, H. Increased fermentability of enzymatically hydrolyzed steam-exploded corn stover for butanol production by removal of fermentation inhibitors. *Process Biochem.* **46,** 604–607 (2011).
34. Chen, C. & Blaschek, H. Acetate enhances solvent production and prevents degeneration in Clostridium beijerinckii BA101. *Appl. Microbiol. Biotechnol.* **52,** 170–3 (1999).
35. Matta-el-Ammouri, G., Janati-Idrissi, R., Junelles, a M., Petitdemange, H. & Gay, R. Effects of butyric and acetic acids on acetone-butanol formation by Clostridium acetobutylicum. *Biochimie* **69,** 109–15 (1987).
36. Oshiro, M., Hanada, K., Tashiro, Y. & Sonomoto, K. Efficient conversion of lactic acid to butanol with pH-stat continuous lactic acid and glucose feeding method by Clostridium saccharoperbutylacetonicum. *Appl. Microbiol. Biotechnol.* **87,** 1177–85 (2010).
37. Ramey, D. E. Continuous two stage, dual path anaerobic fermentation of butanol and other organic solvents using two different strains of bacteria. (1998).
38. Huang, W.-C., Ramey, D. E. & Yang, S. Continuous production of butanol by clostridium acetobutylicum immobilized in a fibrous bed bioreactor. *Appl. Biochem. Biotechnol.* **115,** 887–898 (2004).
39. Afschar, A. S., Biebl, H., Schaller, K., Schiigerl, K. & Schrugerl, K. Production of acetone and butanol by Clostridium acetobutylicum in continuous culture with cell recycle. *Appl Microbiol Biotechnol* **22,** 394–398 (1985).
40. Yang, X. & Tsao, G. T. Enhanced acetone-butanol fermentation using repeated fed-batch operation coupled with cell recycle by membrane and simultaneous removal of inhibitory products by adsorption. *Biotechnol. Bioeng.* **47,** 444–50 (1995).
41. Qureshi, N., Schripsema, J., Lienhardt, J. & Blaschek, H. P. Continuous solvent production by Clostridium beijerinckii BA101 immobilized by adsorption onto brick. *World J. Microbiol. Biotechnol.* **16,** 337–382 (2000).
42. Tashiro, Y., Takeda, K., Kobayashi, G. & Sonomoto, K. High production of acetone-butanol-ethanol with high cell density culture by cell-recycling and bleeding. *J. Biotechnol.* **120,** 197–206 (2005).
43. Lienhardt, J., Schripsema, J., Qureshi, N. & Blaschek, H. P. Butanol production by Clostridium beijerinckii BA101 in an immobilized cell biofilm reactor. *Appl. Biochem. Biotechnol.* **98,** 591–598 (2002).
44. Baba, S.-I., Tashiro, Y., Shinto, H. & Sonomoto, K. Development of high-speed and highly efficient butanol production systems from butyric acid with high density of living cells of Clostridium saccharoperbutylacetonicum. *J. Biotechnol.* 4–11 (2011).
45. Ezeji, T. C., Qureshi, N. & Blaschek, H. P. Production of butanol by Clostridium beijerinckii BA101 and in-situ recovery by gas stripping. *Microbiol. Biotechnol. World J* **19,** 595–603. (2003).
46. Ezeji, T. C., Qureshi, N. & Blaschek, H. P. Butanol fermentation research: Upstream and downstream manipulations. *Chem Rec* **4,** 305–314 (2004).
47. Ezeji, T. C., Qureshi, N. & Blaschek, H. P. Acetone–butanol ethanol (ABE) production from concentrated substrate: Reduction in substrate inhibition by fed-batch technique and product inhibition by gas stripping. *Appl*

Microbiol Biotechnol **63,** 653–658. (2004).

48. Qureshi, N., Meagher, M. M. & Hutkins, R. W. Recovery of butanol from model solutions and fermentation broth using a silicalite/silicone membrane. *J. Memb. Sci.* **158,** 115–125 (1999).
49. Qureshi, N. & Blaschek, H. Butanol production using Clostridium beijerinckii BA101 hyper-butanol producing mutant strain and recovery by pervaporation. *Appl. Biochem. Biotechnol.* **84,** 225–235 (2000).
50. Favre, E., Nguyen, Q. T., Bruneau, S. & Loing, M. S. Extraction of 1 -Butanol from Aqueous Solutions by Pervaporation. **65,** 221–228 (1996).
51. Huang, J. & Meagher, M. M. M. Pervaporative recovery of n-butanol from aqueous solutions and ABE fermentation broth using thin-film silicalite-filled silicone composite membranes. *J. Memb. Sci.* **192,** 231–242 (2001).
52. Groot', W. J., Qever, C. E. & Kossen, N. W. F. Pervaporation for simultaneous product recovery in the butanol/isopropanol batch fermentation. *Biotechnol. Lett.* **6,** 709–714 (1984).
53. Qureshi, N., Meagher, M. M., Huangb, J. & Hutkins, R. W. Acetone butanol ethanol (ABE) recovery by pervaporation using silicalite–silicone composite membrane from fed-batch reactor of Clostridium acetobutylicum. *J. Memb. Sci.* **187,** 93–102 (2001).
54. Park, C. Pervaporative butanol fermentation using a new bacterial strain. *Biotechnol. Bioprocess Eng.* **1,** 1–8 (1996).
55. Izák, P., Schwarz, K., Ruth, W., Bahl, H. & Kragl, U. Increased productivity of Clostridium acetobutylicum fermentation of acetone, butanol, and ethanol by pervaporation through supported ionic liquid membrane. *Appl. Microbiol. Biotechnol.* **78,** 597–602 (2008).
56. Groot, W. J. *et al.* Butanol recovery from fermentations by liquid-liquid extraction and membrane solvent extraction. *Bioprocess Eng.* **5,** 203–216 (1990).
57. Ishizaki, A. Extractive acetone-butanol-ethanol fermentation using methylated crude palm oil as extractant in batch culture of Clostridium saccharoperbutylacetonicum N1-4 (ATCC 13564). *J. Biosci. Bioeng.* **87,** 352–356 (1999).
58. Janke, G. A. & Johnson, Jr., W. D. Extractive fermentation using convoluted fibrous bed bioreactor. (1999).
59. Roffler, S. R., Blanch, H. W. & Wilke, C. R. In-situ recovery of butanol during fermentation. *Bioprocess Eng.* **2,** 181–190 (1987).
60. Job, C., Schertler, C., Staudenbauer, W. L. & Blass, E. Selection of organic solvents for in situ extraction of fermentation products from Clostridium thermohydrosulfuricum cultures. *Biotechnol. Tech.* **3,** 315–320 (1989).
61. Eckert, G., Schügerl, K. & Schiigerl, K. Continuous acetone-butanol production with direct product removal. *Appl. Microbiol. Biotechnol.* **27,** 221–228 (1987).
62. Davison, B. H. & Thompson, J. E. Continuous direct solvent extraction of butanol in a fermenting fluidized-bed bioreactor with immobilized Clostridium acetobutylicum. *Appl. Biochem. Biotechnol.* **39–40,** 415–426 (1993).
63. Qureshi, N. & Maddox, I. S. Reduction in Butanol Inhibition by Perstraction: Utilization of Concentrated Lactose/Whey Permeate by Clostridium acetobutylicum to Enhance Butanol Fermentation Economics. *Food Bioprod. Process.* **83,** 43–52 (2005).
64. Mariano, A. P. *et al.* Dynamics and control strategies for a butanol fermentation process. *Appl. Biochem. Biotechnol.* **160,** 2424–48 (2010).
65. Pinto Mariano, A. *et al.* Optimization Strategies Based on Sequential Quadratic Programming Applied for a Fermentation Process for Butanol Production. *Appl. Biochem. Biotechnol.* **159,** 366–381 (2009).
66. Groot, W. J., van der Lans, R. G. J. M. & Luyben, K. C. A. M. Technologies for butanol recovery integrated with fermentations. *Process Biochem.* **27,** 61–75 (1992).
67. Oudshoorn, A., van der Wielen, L. A. M. & Straathof, A. J. J. Assessment of Options for Selective 1-Butanol Recovery from Aqueous Solution. *Ind. Eng. Chem. Res.* **48,** 7325–7336 (2009).
68. Burns-Guydish *et al.* INTEGRATED BIOREFINERY. **1,** (2013).
69. XU, Y. SYSTEMS AND METHODS FOR ALCOHOL RECOVERY AND CONCENTRATION OF STILLAGE BY-PRODUCTS. (2011).
70. Meagher, M., Qureshi, N. & Hutkins, R. Silicalite membrane and method for the selective recovery and concentration of acetone and butanol from model ABE solutions and fermentation broth. (1998).
71. EVANKO, W. & BROTHERS, M. RECOVERY OF HIGHER ALCOHOLS FROM DILUTE AQUEOUS SOLUTIONS. *WO Patent …* **1,** (2012).
72. FRANK, T. & FERRIO, J. RECOVERY OF VOLATILE PRODUCTS FROM FERMENTATION BROTH. **1,** (2008).
73. Grady, M. C., Parten, W. D., Vrana, B., Xu, Y. T. & Zaher, J. J. Recovery of butanol from a mixture of butanol, water, and an organic extractant. (2013).
74. Kaufman, B., Walther, D. C. & Contag, P. R. Multistage vapor compression distillation. *WO Patent 126848 A1*

(2010).

75. OLLIVIER, F., Rousseaux, P. & CELLIER, C. Improved gas stripping process for the recovery of solvents from fermentation broths. (2011).
76. VITNER, A. A PROCESS FOR THE RECOVERY OF A FERMENTATION PRODUCT. (2009).
77. WALTHER, D. *et al.* INTEGRATED SYSTEM AND PROCESS FOR BIOPRODUCT PRODUCTION. *WO Patent …* (2010).
78. Luyben, W. L. Control of the Heterogeneous Azeotropic n -Butanol/Water Distillation System. *Energy & Fuels* **22,** 4249–4258 (2008).
79. Oudshoorn, A., van den Berg, C., Roelands, C. P. M., Straathof, A. J. J. & van der Wielen, L. a. M. Short-cut calculations for integrated product recovery options in fermentative production of bio-bulk chemicals. *Process Biochem.* **45,** 1605–1615 (2010).
80. Qureshi, N. Agricultural residues and energy crops as potentially economical and novel substrates for microbial production of butanol (a biofuel). *Bioprocess Biosyst. Eng.* (2010). doi:10.1079/PAVSNNR20105059
81. Ferreira, M. C., Meirelles, A. J. a. & Batista, E. a. C. Study of the Fusel Oil Distillation Process. *Ind. Eng. Chem. Res.* **52,** 2336–2351 (2013).
82. Maiti, D., Jana, A. K. & Samanta, A. N. Intensified thermal integration in batch reactive distillation. *Appl. Energy* **103,** 290–297 (2013).
83. Qureshi, N., Saha, B. C., Cotta, M. A. & Singh, V. An economic evaluation of biological conversion of wheat straw to butanol: A biofuel. *Energy Convers. Manag.* **65,** 456–462 (2013).
84. Kharkwal, S., Karimi, I. A., Chang, M. W. & Lee, D. Strain Improvement and Process Development for Biobutanol Production. *Recent Pat. Biotechnol.* **3,** 202–210 (2009).
85. Inui, M. *et al.* Expression of Clostridium acetobutylicum butanol synthetic genes in Escherichia coli. *Appl. Microbiol. Biotechnol.* **77,** 1305–16 (2008).
86. Ezeji, T. C., Qureshi, N. & Blaschek, H. P. No Title. *World J. Microbiol. Biotechnol.* **19,** 595–603 (2003).
87. Vane, L. M. Separation technologies for the recovery and dehydration of alcohols from fermentation broths. *Biofuels, Bioprod. Biorefining* **2,** 553–588 (2008).
88. Mariano, A. P., Qureshi, N., Maciel Filho, R. & Ezeji, T. C. Assessment of in situ butanol recovery by vacuum during acetone butanol ethanol (ABE) fermentation. *J. Chem. Technol. Biotechnol.* **87,** 334–340 (2012).
89. Qureshi, N., Hughes, S., Maddox, I. S. & Cotta, M. A. Energy-efficient recovery of butanol from model solutions and fermentation broth by adsorption. *Bioprocess Biosyst. Eng.* **27,** 215–222 (2005).
90. Chen, Y. *et al.* Enhancement of n-butanol production by in situ butanol removal using permeating–heating–gas stripping in acetone–butanol–ethanol fermentation. *Bioresour. Technol.* **164,** 276–284 (2014).
91. Cai, D. *et al.* Gas stripping–pervaporation hybrid process for energy-saving product recovery from acetone–butanol–ethanol (ABE) fermentation broth. *Chem. Eng. J.* **287,** 1–10 (2016).
92. Kong, X. *et al.* Efficient acetone-butanol-ethanol (ABE) production by a butanol-tolerant mutant of Clostridium beijerinckii in a fermentation-pervaporation coupled process. *Biochem. Eng. J.* **105,** 90–96 (2016).
93. Chen, W.-C. *et al.* Optimizing the efficiency of anhydrous ethanol purification via regenerable molecular sieve. *Appl. Energy* **135,** 483–489 (2014).
94. Vane, L. & Alvarez, F. Liquid Separation by membrane assisted vapor stripping process. (2013).
95. Kiss, A. a. & Suszwalak, D. J.-. P. C. Enhanced bioethanol dehydration by extractive and azeotropic distillation in dividing-wall columns. *Sep. Purif. Technol.* **86,** 70–78 (2012).
96. Vázquez-Ojeda, M., Segovia-Hernández, J. G. & Ponce-Ortega, J. M. Incorporation of Mass and Energy Integration in the Optimal Bioethanol Separation Process. *Chem. Eng. Technol.* **36,** 1865–1873 (2013).
97. Figueroa, J. J., Lunelli, B. H., Filho, R. M. & Maciel, M. R. W. Improvements on Anhydrous Ethanol Production by Extractive Distillation using Ionic Liquid as Solvent. *Procedia Eng.* **42,** 1016–1026 (2012).
98. Gil, I., Uyazan, A. & Aguilar, J. Separation of ethanol and water by extractive distillation with salt and solvent as entrainer: process simulation. *Brazilian J. Chem. Eng.* **25,** 207–215 (2008).
99. Dias, M. O. S., Junqueira, T. L., Maciel Filho, R., Maciel, M. R. W. & Eduardo Vaz Rossell, C. in *19th European Symposium on Computer Aided Process Engineering – ESCAPE1* 519–524 (2009). doi:10.1016/S1570-7946(09)70087-2
100. Lee, F.-M. *et al.* Low-energy extractive distillation process for dehydration of aqueous ethanol. (2012).
101. de Figueirêdo, M. F., Guedes, B. P., de Araújo, J. M. M., Vasconcelos, L. G. S. & Brito, R. P. Optimal design of extractive distillation columns—A systematic procedure using a process simulator. *Chem. Eng. Res. Des.* **89,** 341–346 (2011).

102. Matsuda, K. *et al.* Advanced energy saving in distillation process with self-heat recuperation technology. *Energy* **36,** 4640–4645 (2011).
103. Kiran, B., Jana, A. K. & Samanta, A. N. A novel intensified heat integration in multicomponent distillation. *Energy* **41,** 443–453 (2012).
104. Kiss, A. a. & Ignat, R. M. Enhanced methanol recovery and glycerol separation in biodiesel production – DWC makes it happen. *Appl. Energy* **99,** 146–153 (2012).
105. Yildirim, Ö., Kiss, A. a. & Kenig, E. Y. Dividing wall columns in chemical process industry: A review on current activities. *Sep. Purif. Technol.* **80,** 403–417 (2011).
106. Bessa, L. C. B. A., Ferreira, M. C., Batista, E. A. C. & Meirelles, A. J. A. Performance and cost evaluation of a new double-effect integration of multicomponent bioethanol distillation. *Energy* **63,** 1–9 (2013).
107. Bessa, L. C. B. a., Batista, F. R. M. & Meirelles, A. J. a. Double-effect integration of multicomponent alcoholic distillation columns. *Energy* **45,** 603–612 (2012).
108. You, X., Rodriguez-Donis, I. & Gerbaud, V. Reducing process cost and CO2emissions for extractive distillation by double-effect heat integration and mechanical heat pump. *Appl. Energy* **166,** 128–140 (2016).
109. Mulia-Soto, J. F. & Flores-Tlacuahuac, A. Modeling, simulation and control of an internally heat integrated pressure-swing distillation process for bioethanol separation. *Comput. Chem. Eng.* **35,** 1532–1546 (2011).
110. Luo, H., Bildea, C. S. & Kiss, A. a. Novel Heat-Pump-Assisted Extractive Distillation for Bioethanol Purification. *Ind. Eng. Chem. Res.* **54,** 2208–2213 (2015).
111. Kiss, A. A. & Ignat, R. M. Innovative single step bioethanol dehydration in an extractive dividing-wall column. *Sep. Purif. Technol.* **98,** 290–297 (2012).
112. Ramírez-Márquez, C., Segovia-Hernández, J. G., Hernández, S., Errico, M. & Rong, B. Dynamic Behavior of Alternative Separation Processes for Ethanol Dehydration by Extractive Distillation. *Ind. Eng. Chem. Res.* **52,** 17554–17561 (2013).
113. Babu, G. U. B., Aditya, R. & Jana, A. K. Economic feasibility of a novel energy efficient middle vessel batch distillation to reduce energy use. *Energy* **45,** 626–633 (2012).
114. Douglas, J. M. *Conceptual design of chemical processes*. (1988).
115. Ruggeri, B., Tommasi, T. & Sanfilippo, S. *BioH2 & BioCH4 Through Anaerobic Digestion*. (Springer London, 2015). doi:10.1007/978-1-4471-6431-9
116. Vane, L. M. & Alvarez, F. R. Hybrid vapor stripping-vapor permeation process for recovery and dehydration of 1-butanol and acetone/butanol/ethanol from dilute aqueous solutions. Part 1. Process Simulations. *J. Chem. Technol. Biotechnol.* **88,** 1436–1447 (2013).
117. Marongiu, B., Ferino, I., Monaci, R., Solinas, V. & Torrazza, S. Thermodynamic properties of aqueous non-electrolyte mixtures. Alkanols + + water systems. *J. Mol. Liq.* **28,** 229–247 (1984).
118. Zhang, Y.; Fu, J.; Zhang, J. Liquid-Liquid Equilibrium and Vapor-Liquid Equilibrium for Containing Octylenic Aldehyde Systems. *J. Chem. Ind. Eng.* **43,** 98–104 (1992).
119. Al-Sahhaf, T. A. & Jabbar, N. J. Vapor-liquid equilibrium of the acetone-water-salt system. *J. Chem. Eng. Data* **38,** 522–526 (1993).
120. Reinders, W. & de Minjer, C. H. Vapour-liquid equilibria in ternary systems. VI. The system water-acetone-chloroform. *Recl. des Trav. Chim. des Pays-Bas* **66,** 573–604 (1947).
121. Othmer, D. F., Chudgar, M. M. & Levy, S. L. Binary and Ternary Systems of Acetone, Methyl Ethyl Ketone, and Water. *Ind. Eng. Chem.* **44,** 1872–1881 (1952).
122. Vane, L. M., Alvarez, F. R., Rosenblum, L. & Govindaswamy, S. Hybrid vapor stripping-vapor permeation process for recovery and dehydration of 1-butanol and acetone/butanol/ethanol from dilute aqueous solutions. Part 2. Experimental validation with simple mixtures and actual fermentation broth. *J. Chem. Technol. Biotechnol.* **88,** 1436–1447 (2013).
123. Annous, B. A. & Blaschek, H. P. Isolation and characterization of Clostridium acetobutylicum mutants with enhanced amylolytic activity. *Appl. Environ. Microbiol.* **57,** 2544–8 (1991).
124. Mariano, A. P. *et al.* Energy Requirements for Butanol Recovery Using the Flash Fermentation Technology. *Energy & Fuels* **25,** 2347–2355 (2011).
125. Nicolaou, S. a., Gaida, S. M. & Papoutsakis, E. T. A comparative view of metabolite and substrate stress and tolerance in microbial bioprocessing: From biofuels and chemicals, to biocatalysis and bioremediation. *Metab. Eng.* **12,** 307–331 (2010).
126. Lu, C., Zhao, J., Yang, S.-T. & Wei, D. Fed-batch fermentation for n-butanol production from cassava bagasse hydrolysate in a fibrous bed bioreactor with continuous gas stripping. *Bioresour. Technol.* **104,** 380–7 (2012).
127. Mariano, A. P. & Filho, R. M. Improvements in Biobutanol Fermentation and Their Impacts on Distillation Energy Consumption and Wastewater Generation. *Bioenergy Res.* **5,** 504–514 (2012).

128. Veloo, P. S., Wang, Y. L., Egolfopoulos, F. N. & Westbrook, C. K. A comparative experimental and computational study of methanol, ethanol, and n-butanol flames. *Combust. Flame* **157,** 1989–2004 (2010).

129. Xue, C., Zhao, X. Q., Liu, C. G., Chen, L. J. & Bai, F. W. Prospective and development of butanol as an advanced biofuel. *Biotechnol. Adv.* **31,** 1575–1584 (2013).

130. González-Peñas, H., Lu-Chau, T. A., Moreira, M. T. & Lema, J. M. Assessment of morphological changes of Clostridium acetobutylicum by flow cytometry during acetone/butanol/ethanol extractive fermentation. *Biotechnol. Lett.* 577–584 (2014). doi:10.1007/s10529-014-1702-3

131. Kraemer, K., Harwardt, A., Bronneberg, R. & Marquardt, W. Separation of butanol from acetone–butanol–ethanol fermentation by a hybrid extraction–distillation process. *Comput. Chem. Eng.* **35,** 949–963 (2011).

132. Kurkijärvi, A., Lehtonen, J. & Linnekoski, J. Novel dual extraction process for acetone-butanol-ethanol fermentation. *Sep. Purif. Technol.* **124,** 18–25 (2014).

133. Evans, P. J. & Wang, H. Y. Enhancement of Butanol Formation by Clostridium acetobutylicum in the Presence of Decanol-Oleyl Alcohol Mixed Extractants. *Appl. Environ. Microbiol.* **54,** 1662–7 (1988).

134. Bankar, S. B., Survase, S. a., Singhal, R. S. & Granström, T. Continuous two stage acetone–butanol–ethanol fermentation with integrated solvent removal using Clostridium acetobutylicum B 5313. *Bioresour. Technol.* **106,** 110–116 (2012).

135. Fischer, K. & Gmehling, J. P-x and .gamma..infin. Data for the Different Binary Butanol-Water Systems at 50.degree.C. *J. Chem. Eng. Data* **39,** 309–315 (1994).

136. Ni, Y. & Sun, Z. Recent progress on industrial fermentative production of acetone–butanol–ethanol by Clostridium acetobutylicum in China. *Appl. Microbiol. Biotechnol.* **83,** 415–423 (2009).

137. Kim, Y. H. Side-rectifier divided wall column for offshore LNG plant. *Sep. Purif. Technol.* **139,** 25–35 (2015).

138. Zauba. India's import and export data. *https://www.zauba.com/* (2015).

139. Mussatto, S. I., Moncada, J., Roberto, I. C. & Cardona, C. a. Techno-economic analysis for brewer's spent grains use on a biorefinery concept: The Brazilian case. *Bioresour. Technol.* **148,** 302–310 (2013).

140. Köhler, K. A. K., Rühl, J., Blank, L. M. & Schmid, A. Integration of biocatalyst and process engineering for sustainable and efficient n -butanol production. *Eng. Life Sci.* **15,** 4–19 (2015).

141. Kurkijärvi, A. J. & Lehtonen, J. Dual Extraction Process for the Utilization of an Acetone–Butanol–Ethanol Mixture in Gasoline. *Ind. Eng. Chem. Res.* **53,** 12379–12386 (2014).

142. Roffler, S. R., Blanch, H. W. & Wilke, C. R. In situ extractive fermentation of acetone and butanol. *Biotechnol. Bioeng.* **31,** 135–143 (1988).

143. Ezeji, T., Qureshi, N. & Blaschek, H. P. Butanol production from agricultural residues: Impact of degradation products on Clostridium beijerinckii growth and butanol fermentation. *Biotechnol. Bioeng.* **97,** 1460–9 (2007).

144. Qureshi, N. *et al.* Effect of cellulosic sugar degradation products (furfural and hydroxymethyl furfural) on acetone-butanol-ethanol (ABE) fermentation using Clostridium beijerinckii P260. *Food Bioprod. Process.* **90,** 533–540 (2012).

145. Chen, M. L. & Wang, F. S. Optimization of a fed-batch simultaneous saccharification and cofermentation process from lignocellulose to ethanol. *Ind. Eng. Chem. Res.* **49,** 5775–5785 (2010).

146. Chandel, A. K. *et al.* in *D-Xylitol* (eds. da Silva, S. S. & Chandel, A. K.) 39–61 (Springer Berlin Heidelberg, 2012). doi:10.1007/978-3-642-31887-0_2

147. Andrić, P., Meyer, A. S., Jensen, P. a & Dam-Johansen, K. Reactor design for minimizing product inhibition during enzymatic lignocellulose hydrolysis: II. Quantification of inhibition and suitability of membrane reactors. *Biotechnol. Adv.* **28,** 407–25 (2010).

148. Qureshi, N. *et al.* Process integration for simultaneous saccharification, fermentation, and recovery (SSFR): production of butanol from corn stover using Clostridium beijerinckii P260. *Bioresour. Technol.* **154,** 222–8 (2014).

149. Zhu, Y. & Yang, S.-T. Effect of pH on metabolic pathway shift in fermentation of xylose by Clostridium tyrobutyricum. *J. Biotechnol.* **110,** 143–57 (2004).

150. Tanaka, S. *et al.* Membrane-assisted extractive butanol fermentation by Clostridium saccharoperbutylacetonicum N1-4 with 1-dodecanol as the extractant. *Bioresour. Technol.* **116,** 448–52 (2012).

151. Shinto, H. *et al.* Kinetic study of substrate dependency for higher butanol production in acetone–butanol–ethanol fermentation. *Process Biochem.* **43,** 1452–1461 (2008).

152. Shinto, H. *et al.* Kinetic modeling and sensitivity analysis of acetone-butanol-ethanol production. *J. Biotechnol.* **131,** 45–56 (2007).

153. Zheng, J., Tashiro, Y., Wang, Q., Sakai, K. & Sonomoto, K. Feasibility of acetone–butanol–ethanol fermentation from eucalyptus hydrolysate without nutrients supplementation. *Appl. Energy* **140,** 113–119 (2015).

154. Kadam, K. L., Rydholm, E. C. & McMillan, J. D. Development and validation of a kinetic model for enzymatic saccharification of lignocellulosic biomass. *Biotechnol. Prog.* **20,** 698–705 (2004).
155. Hu, S. *et al.* A novel method for furfural recovery via gas stripping assisted vapor permeation by a polydimethylsiloxane membrane. *Sci. Rep.* **5,** 9428 (2015).
156. Fadeev, a G. *et al.* Extraction of butanol from aqueous solutions by pervaporation through poly(1-trimethylsilyl-1-propyne). *J. Memb. Sci.* **186,** 205–217 (2001).
157. Claes, S. *et al.* Preparation and benchmarking of thin film supported PTMSP-silica pervaporation membranes. *J. Memb. Sci.* **389,** 265–271 (2012).
158. Liu, X. *et al.* Capillary supported ultrathin homogeneous silicalite-poly(dimethylsiloxane) nanocomposite membrane for bio-butanol recovery. *J. Memb. Sci.* **369,** 228–232 (2011).
159. Dong, Z., Liu, G., Liu, S., Liu, Z. & Jin, W. High performance ceramic hollow fiber supported PDMS composite pervaporation membrane for bio-butanol recovery. *J. Memb. Sci.* **450,** 38–47 (2014).
160. Matsumura, M., Takehara, S. & Kataoka, H. Continuous butanol/isopropanol fermentation in down-flow column reactor coupled with pervaporation using supported liquid membrane. *Biotechnol. Bioeng.* **39,** 148–156 (1992).
161. Thongsukmak, A. & Sikar, K. K. Pervaporation membranes highly selective for solvents present in fermentation broths. *J. Memb. Sci.* **302,** 45–58 (2007).
162. Baker, R. W., Wijmans, J. G. & Huang, Y. Permeability, permeance and selectivity: A preferred way of reporting pervaporation performance data. *J. Memb. Sci.* **348,** 346–352 (2010).
163. Dubreuil, M. F. S., Vandezande, P., Van Hecke, W. H. S., Porto-Carrero, W. J. & Dotremont, C. T. E. Study on ageing/fouling phenomena and the effect of upstream nanofiltration on in-situ product recovery of n-butanol through poly[1-(trimethylsilyl)-1-propyne] pervaporation membranes. *J. Memb. Sci.* **447,** 134–143 (2013).
164. Sánchez-Ramírez, E., Quiroz-Ramírez, J. J., Segovia-Hernández, J. G., Hernández, S. & Bonilla-Petriciolet, A. Process Alternatives for Biobutanol Purification: Design and Optimization. *Ind. Eng. Chem. Res.* **54,** 351–358 (2015).
165. Zhang, Y. & Ezeji, T. C. Elucidating and alleviating impacts of lignocellulose-derived microbial inhibitors on Clostridium beijerinckii during fermentation of Miscanthus giganteus to butanol. *J. Ind. Microbiol. Biotechnol.* 1505–1516 (2014). doi:10.1007/s10295-014-1493-5
166. Jeong, G. T., Kim, S. K. & Park, D. H. Detoxification of hydrolysate by reactive-extraction for generating biofuels. *Biotechnol. Bioprocess Eng.* **18,** 88–93 (2013).
167. Lee, S., Lee, J. H. & Mitchell, R. J. Analysis of Clostridium beijerinckii NCIMB 8052's transcriptional response to ferulic acid and its application to enhance the strain tolerance. *Biotechnol. Biofuels* **8,** 68 (2015).
168. Matsumura, M., Kataoka, H., Sueki, M. & Araki, K. Energy saving effect of pervaporation using oleyl alcohol liquid membrane in butanol purification. *Bioprocess Eng.* **3,** 93–100 (1988).
169. González-Peñas, H., Lu-Chau, T. a., Moreira, M. T. & Lema, J. M. Solvent screening methodology for in situ ABE extractive fermentation. *Appl. Microbiol. Biotechnol.* **98,** 5915–5924 (2014).
170. van der Merwe, A. B., Cheng, H., Görgens, J. F. & Knoetze, J. H. Comparison of energy efficiency and economics of process designs for biobutanol production from sugarcane molasses. *Fuel* **105,** 451–458 (2013).
171. Liu, J., Fan, L. T., Seib, P., Friedler, F. & Bertok, B. Downstream process synthesis for biochemical production of butanol, ethanol, and acetone from grains: generation of optimal and near-optimal flowsheets with conventional operating units. *Biotechnol. Prog.* **20,** 1518–27 (2004).
172. Ghanadzadeh, H. & Ghanadzadeh, A. Liquid−Liquid Equilibria of Water + 1-Butanol + 2-Ethyl-1-hexanol System. *J. Chem. Eng. Data* **49,** 783–786 (2004).
173. Ghanadzadeh, H., Ghanadzadeh, a. & Sariri, R. (Liquid+liquid) equilibria for (water+acetic acid+2-ethyl-1-hexanol): experimental data and prediction. *J. Chem. Thermodyn.* **36,** 1001–1006 (2004).
174. Ghanadzadeh, H. & Ghanadzadeh, a. (Liquid+liquid) equilibria in (water+ethanol+2-ethyl-1-hexanol) at T=(298.2, 303.2, 308.2, and 313.2) K. *J. Chem. Thermodyn.* **35,** 1393–1401 (2003).
175. Ghanadzadeh, H., Ghanadzadeh, A. & Alitavoli, M. LLE of ternary mixtures of water/acetone/2-ethyl-1-hexanol at different temperatures. *Fluid Phase Equilib.* **219,** 165–169 (2004).
176. Davis, R. *et al.* Process Design and Economics for the Conversion of Lignocellulosic Biomass to Hydrocarbons: Dilute-Acid and Enzymatic Deconstruction of Biomass to Sugars and Biological Conversion of Sugars to Hydrocarbons. *Natl. Renew. Energy Lab.* 147 (2013). doi:10.2172/1107470
177. Li, J. *et al.* Efficient production of acetone–butanol–ethanol (ABE) from cassava by a fermentation–pervaporation coupled process. *Bioresour. Technol.* **169,** 251–257 (2014).
178. Nandong, J., Engineering, C., Samyudia, Y. & Tadé, M. O. Chemical Product and Process Dynamic Simulation and Optimization of Two-Stage Extractive Alcoholic Fermentation Process : Design Impact on Controllability Dynamic Simulation and Optimization of Two-Stage Extractive Alcoholic Fermentation Process : Design . **1,**

(2006).
179. Humbird, D. *et al.* Process Design and Economics for Biochemical Conversion of Lignocellulosic Biomass to Ethanol. *Natl. Renew. Energy Lab.* (2011).
180. Luyben, W. L. & Chien, I. L. *Design and Control of Distillation Systems for Separating Azeotropes*. *Design and Control of Distillation Systems for Separating Azeotropes* (2010). doi:10.1002/9780470575802
181. Pretreatment, D. Process Design and Economics for Biochemical Conversion of Lignocellulosic Biomass to Ethanol Process Design and Economics for Biochemical Conversion of Lignocellulosic Biomass to Ethanol. *Natl. Renew. Energy Lab.* (2011).
182. Abrams, D. S. & Prausnitz, J. M. Statistical thermodynamics of liquid mixtures: A new expression for the excess Gibbs energy of partly or completely miscible systems. *AIChE J.* **21,** 116–128 (1975).
183. Winkelman, J. G. M., Kraai, G. N. & Heeres, H. J. Binary, ternary and quaternary liquid–liquid equilibria in 1-butanol, oleic acid, water and n-heptane mixtures. *Fluid Phase Equilib.* **284,** 71–79 (2009).
184. Boluda, N., Gomis, V., Ruiz, F. & Bailador, H. The influence of temperature on the liquid–liquid–solid equilibria of the ternary system water+ethanol+1-dodecanol. *Fluid Phase Equilib.* **235,** 99–103 (2005).
185. Kirbaslar, S. & Cehreli, S. Equilibrium data on water-ethanol-1-dodecanol ternary system. *Turk. J. Engin. …* **25,** 111–115 (2001).
186. Henley, E., Seader, J. & Roper, D. *Separation process principles*. (2011).