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Optimal design of an efficient, profitable and sustainable biorefinery producing acetone, butanol and ethanol: Influence of the *in-situ* separation on the purification structure

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A B S T R A C T

The bio-based *n*-butanol has major potential to replace fossil-based products due to, on the first hand, the decline of crude oil and, on the other hand, since the butanol has high potential as fuel. To set its production in industrial scale the development of tools designing the process is needed. In our work, we focus on second generation biorefinery using wood as feedstock. The biorefinery was composed by the pretreatment, the hydrolysis, the fermentation, the butanol recovery and the purification. The proposed methodology is a multiscale decision support tool for the selection of the optimal process design of the biorefinery producing biobutanol. The optimal biorefinery is selected from the superstructure recapping all feasible scenarios after process modelling and simulation, economic and environmental evaluations and energy integration. Thus, the optimal process is profitable, efficient and sustainable. Moreover, to identify the influence of the biobutanol recovery on the fermentation's performances, the process modelling includes the retroaction of biobutanol recovery. In this study, three biobutanol recovery and four purification scenarios are combined and then processes are compared to select the optimal biorefinery for the bio based butanol production.

Keywords:

Bioprocess design
Downstream processing
Modelling
Process integration
Optimal design
Biobutanol

1. Introduction

Among biofuel possibilities, bioethanol was the most studied and produced because of its ease of conversion at industrial scale. However butanol has also a high potential as biofuel because of its relevant, favorable physico-chemical properties [1], which are very similar to fuel's ones, as illustrated on Table 1.

Then, any fuel-butanol blended up to a 100% butanol can be utilized in fuel engines without modification of technology [4] and, butanol has also higher energy content than ethanol. Furthermore, butanol has other utilizations [5]: solvent in paints and coatings, chemical building block for the production of several products like polymers such as polypropylene, 1-butene, and intermediate for the production of more complex molecules. As a consequence, in the context of bio-based economy development, it is interesting to produce butanol from renewable resources, and more particularly from biomass.

Historically, from the early twentieth century *n*-butanol was produced *via* the acetone-butanol-ethanol (ABE) fermentation

with bacteria such as *Clostridium* type. According to the study of Niemistö et al. [6], the industrial production started at around 1920. However, as soon as the petrochemical production was developed, ABE fermentation was forsaken. Interest in the bio-based butanol only reappeared in the 2000s due to the awareness of the issues of global warming and climate change, but mainly due to the need of alternatives to fossil-based butanol because of the decline of petroleum resources. Currently, many researches focus on the ABE fermentation in many different topics (see Section 2): the genetic engineering to describe new pathways or genetic modifications in order to improve productivity of microorganisms, the bioprocess to elaborate new processes to improve performances of fermentation, etc. However, very few research studies focus on the global process of biorefinery and especially on the biobutanol production [7–9]. Indeed, the industrial development of bio-based butanol needs the thorough study of potential processes to ascertain the economic and ecological viability of these biorefineries. Actually, there are many processes for the production of butanol depending on the feedstock, and in our case we use the ABE fermentation. It consists in the conversion of renewable carbon-based raw materials into bioproducts through a sequence of thermal, physical, chemical and biological steps. Nowadays, three generations of biorefinery were identified according to the feedstocks used [10,11]: the first generation converts starches e.g. corn and sugars beets, the sec-

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Table 1
Comparison between physic-chemical properties of diesel fuel, gasoline, ethanol and *n*-butanol [2,3].

Properties	<i>n</i> -Butanol	Ethanol	Gasoline	Diesel fuel
Lower caloric value (MJ/L)	29.2	21.2	32.5	39
Cetane number	25	8	///	50
Heat of vaporization (MJ/kg)	0.43	0.92	0.36	0.25
Research octane number	96	129	91–99	///
Motor octane number	78	102	81–89	///
Air-fuel ratio	11.2	9	14.6	15
Solubility in water	Immiscible	Miscible	Immiscible	Immiscible

ond generation focuses on lignocellulosic feedstocks like wood and the third generation uses algae. These biomasses can come from agriculture, industrial and households wastes or forestry. In this study, we will focus on the production of bio-based butanol *via* the transformation of wood, because of its world wide availability and the large amount of woody wastes rejected in paper industry. Thus, the reuse of these wastes as raw materials allows creating a circular economy and limiting the natural resources exploitation.

Furthermore, a huge amount of laboratory data about the biobutanol production exists but to create real biorefineries, it is necessary to find methods to reconcile laboratory and the industrial scale. In this way, the methodologies combining process optimization and process design have a high potential. Their function consists in establishing process alternatives, the verification of feasibility, the generation of knowledge on the structural model (topology of the process) and the behavioral model (operating parameters) and finally the determination of the optimal process design and process parameters in order to improve profitability while respecting the desired production quantity, the required quality of product, etc. Various researches [12–16] proposed optimization tools for the process design at various scales of study, for example, method and tools at the supply chain level focus on macroscopic topics like the spatial and time-related aspects, the LCA (Life Cycle Analysis) of the process, network of biorefineries, logistic and variations in markets.

Concerning the biorefinery scale, and more especially the four steps that compose a biorefinery (pretreatment and hydrolysis of feedstock, fermentation, separation or butanol recovery and purification) a two-stages approach for the synthesis and the optimization of biorefineries configuration was proposed by Pham and El-Halwagi [17]: the first step established the potential final bioproducts through possible pathways from several fixed feedstock, and then the second step optimized the process in function on the economic and process performances of the biorefinery. Nevertheless, this method focus on the conversion pathway, consequently the pretreatments, the separations and the purifications

are not considered. The optimization model of Moncada et al. [18] established the biorefinery's optimal configuration with respect to the economic, environmental and technical objectives to produce biochemical products and bioenergy. The different biochemical pathways are simulated to obtain accurate mass and energy balances and then compared, but the entire process is not studied. We underline that the model is applied for a specific geographic area with the aim to include the local economic policy of a country. Sammons Jr. et al. [19] focused on the maximization of the Net Present Value (NPV) and the minimization of the ecological impact through empiric calculations. This model includes energy integration (Pinch method) and the use of green solvents in the process. To simplify the calculation, they created a library of processes based on experimental data and process simulation. Zondervan et al. [20] proposed a black box model determining the optimal multiproduct biorefinery from a superstructure. Their Mixed Integer Nonlinear Programming (MINLP) model minimizes costs, maximizes yields and minimizes wastes in order to determine the optimal pathway for each bioproduct. Moreover, it calculates the optimal allocation of several feedstocks for each pathway. However, the calculation of separations is based on separation factors, thus the influence of the thermodynamic is not modeled. Geraili et al. [21] proposed a tool based on the superstructure of a multiproduct biorefinery. Their Linear Programming model determined the optimal process after process simulation with complex kinetics and some optimizations of operating conditions. The objectives are mainly the maximization of the production and the NPV, therefore either environmental criterion or energy integration are considered.

Some researches focus on the integrated biorefinery, and more especially on the integration of energy or water networks, two of the most important operating costs in a biorefinery. The work of Grossmann and Martín [22] aimed to the minimization of energy and water consumptions in first and second generation of biorefinery producing bioethanol. They proposed a two-steps model which minimalizes energy consumption by designing the biorefinery from a superstructure with a MINLP model, and then optimizes water network to minimize freshwater. They proposed a very complete superstructure which encompasses the new technological breakthrough in the domain.

Nevertheless, in addition to the energy consumption, the separation step is another preponderant issue for the production of biobutanol because the fermentation and the separation are coupled in order to improve the fermentation performances. Therefore, the combination of fermentation and separation must represent a large part of the analysis. Some researches interested to this issue. For example, Zondervan et al. [20] studied biorefinery alternatives for the production of ethanol, butanol, acetone and succinic

Table 2
Characteristics of Clostridia bacteria.

Bacterium	<i>C. acetobutylicum</i>	<i>C. beijerinckii</i>	<i>C. saccharobutylicum</i>	<i>C. saccharoperbutylacetonicum</i>
Studied range of temperature (°C)	30–37	30–37	35–37	30
Studied range of pH	4.3–6.5	4.7–6.5	4.5–6.5	5.5–6.5
Dilution rate (h ⁻¹)	0.287	0.07	0.13	0.20
ABE Productivity (g/(L.h))	2.08	0.58	0.85	1.85
Acids productivity (g/(L.h))	0.861	0.175	0.13	N/A
ABE Concentration (g/L)	7.25	8.29	7.74	9.27
Acids Concentration (g/L)	3.0	2.5	1.17	N/A
Consummed substrates	Glucose, xylose, arabinose, mannose, cellobiose, galactose, starch, lactose, sucrose, fructose, lactose, maltose	Glucose, xylose, arabinose, cellobiose, mannose, galactose, starch, sucrose, fructose, maltodextrin, sorbitol, mannitol	Glucose, xylose, arabinose, cellobiose, mannose, galactose	Glucose, starch, maltose, molasses
References	[28–31]	[31–34]	[31,34,35]	[31,36,37]

N/A: no information.

Table 3
Some properties of pine wood.

Compound		Typical dry matter content (%/w DM) [38]	Formula
Cellulose		44.55	C ₆ H ₁₀ O ₅
Hemicellulose	Xylan	6.30	C ₅ H ₈ O ₄
	Arabinan	1.60	C ₅ H ₈ O ₄
	Galactan	2.56	C ₆ H ₁₀ O ₅
	Mannan	11.43	C ₆ H ₁₀ O ₅
Lignin		27.67	C ₁₀ H _{13.9} O _{1.3}
Other		5.87	C ₂ H ₄ O ₂

acid. But, their model did not address the issue of the feasibility of the process for high purity because results are extrapolated from process simulation and laboratory data. Moreover, the objectives (minimization of costs of chemicals used in the processing routes and maximization of product yields) do not insure the profitability of the biorefinery. Some studies focused more on the separation and purification steps. Fan et al. [23] established the superstructure of the separation and purification steps and then determined the optimal process in evaluating economic performances to create an economically viable biorefinery. In this way, process simulation is used in order to calculate the different costs of the process. We emphasize that the superstructure comprises also a scenario without separation and the scenarios with the new technologies for the butanol recovery. Moreover, Stoffers et al. [24] modeled several alternatives of separations for the purification of only the biobutanol and compared them in function of the purification cost of biobutanol. They proved that the extraction alternative presents lower purification cost than pure distillation alternative. Nevertheless, the costs of extraction and pervaporation alternatives could decrease significantly with energy integration. van der Merwe et al. [25] compared several purification alternatives by simulation. However, comparison remained difficult nay impossible because they used different microorganisms in each scenario, thus the input stream of purification steps are different. Finally, Errico et al. [26] chose a Differential Evolution with Tabu List method for the optimization of the purification step. The model is based on process simulation, economic objective and environmental constraints. These previous studies agree that a separation phase before the purification is necessary to limit energy consumption. Nevertheless, none of the presented model includes the retroaction of the butanol recovery on the fermentation whereas this phenomenon is preponderant in the process.

According to the optimization methods for the process design of biorefineries and especially biorefineries producing butanol [18–21,26], each model deals with some objectives but it does not exist a complete method that integrate all the steps of a biorefinery. Moreover, no method includes the retroaction of the butanol recovery on the performances of the fermentation. As a consequence, in this study, a complete and multiscale methodology for the optimal design of the biorefinery producing biobutanol was proposed to fill this gap. This method is a decision support tool based on several objectives: efficiency, profitability and sustainability. The competitiveness of biobutanol is ascertained by the determination of the selling price of butanol in order to compare it with the price of fossil-based butanol. Moreover, the method focused on the separation and purification steps in including the influence of the butanol recovery on the fermentation through the process modelling and simulation.

The methodology comprises the building of the superstructure capitalizing all potential alternatives for the biobutanol production and it focuses especially on the butanol recovery and purification steps. First, process modelling and simulation of all alternatives allowed calculating accurate mass and energy balances due to the complex thermodynamic background. Second, the tool assesses

economic and environmental performances for each alternative and compared them in order to determine the most efficient, the most profitable and the less polluting process. The comparison is realized according to three scenarios: the comparison of separation alternatives with fixed purification, the comparison of purification alternatives with fixed separation and the comparison of all alternatives. Furthermore, in the proposed methodology, energy integration is performed on processes to reduce utilities consumption.

The remainder of this paper is structured as follows. In Section 2, the different steps of the methodology for the multiscale modelling and optimization of biorefineries producing biobutanol are detailed. The Section 3 highlights the results and discussions about the optimization on the ABE production. Finally, conclusions on the biobutanol production are drawn and some perspectives are proposed for future studies.

2. Methodology

In this section, the proposed generic methodology for the optimal design of biorefinery is explained in details with example of the ABE production from woody biomass. The methodology is illustrated in Fig. 1 and as it can be seen, it is divided into 9 steps.

We underlined that the proposed methodology included a multi-scale integration: it grows from molecule scale to biorefinery scale, including unit operation and process scales, and each level interacts with others repetitively by exchanging information or data. The thermodynamic and microbiological data at the molecule scale are used to describe the different unit operations composing the different process operations. Then, during the calculation, we can iterate on the different scales, *i.e.* molecule, unit operation, process and biorefinery scales, in function of the required data.

2.1. Creation of a feasible and realistic superstructure

First, the methodology starts with the creation of the superstructure of the biorefinery producing biobutanol. However, some proposed processes cannot produce bioproducts with the required quality or some successions of unit operations are not possible for example due to thermodynamics constraints. In order to insure the feasibility, each process alternative was modeled and simulated with the process modelling software *Aspen Plus 8.6*[®].

We remark that the unit operation scale is crucial in the model due to its key position in the multiscale approach, *i.e.* it ensures the link between the process scale constraints and the experimental data extracted from the molecule scale. Furthermore, the unit operation scale will serve to calculate accurate results based on complex equations instead of stating hypothesis used in the traditional black box model.

2.1.1. Bioproducts specificities and microorganisms

2.1.1.1. Step 1—the bioproducts. To use biobutanol and bioethanol as biofuels, their purity is fixed at 99.7% w/w, it corresponds to the required purity for bioethanol according to European laws. Moreover, the quality of acetone is fixed at 99.9% w/w that corresponds to extra pure acetone (high quality solvent mainly used in cosmetic industry). These purities match with the highest industrial purities to consider the most constrained scenarios.

2.1.1.2. Step 2—inventory of microorganisms for the fermentation ABE. The bacteria producing butanol belong to the class Clostridia. Thanks to the genetic engineering, from the different Clostridia bacteria species, the four most important have been identified [27]: *Clostridium acetobutylicum*, *Clostridium beijerinckii*, *Clostridium saccharobutylicum* and *Clostridium saccharoperbutylacetonicum*. Table 2 details the characteristics of these bacteria. All

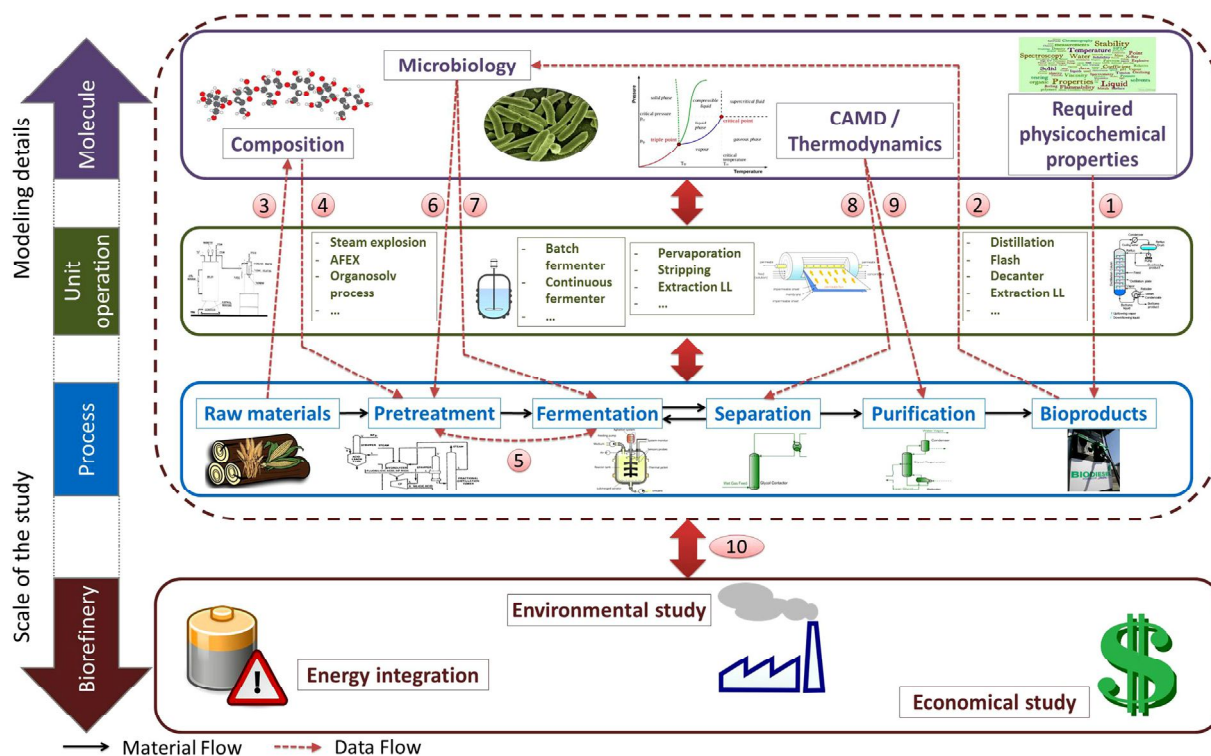


Fig. 1. Representation of the multi-scale decision support tool for the design and the optimization of biorefineries.

bacteria presented in Table 2 are able to transform the pentoses and hexoses into biobutanol under specific operating conditions.

For each bacterium, the fermentation produces butanol as main product and acetone and ethanol as byproducts. Moreover, acids (acetic acid and butyric acid) are frequently observed in the fermentation broth. Indeed, they are reactive intermediate during the fermentation. According to Table 2, whatever the bacterium, the ranges of operating conditions (temperature and pH) are similar. Moreover, bacterium *C. acetobutylicum* presents the highest productivity (2.08 g/(Lh)) and consumes many different substrates including hexoses and pentoses. Consequently, we select this bacterium for the fermentation step of the transformation process. Nevertheless, the productivity of acids of 0.861 g/(Lh) is not negligible, then acids must be considered in the fermentation kinetics.

2.1.2. Pretreatment and hydrolysis

2.1.2.1. Step 3—the feedstock. In this study, the selected feedstock is woody biomass. The biorefinery is located in the French southwest where pine is one of the common tree species because of its fast growth. The dry matter content of pine is detailed in Table 3. To obtain an industrial size biorefinery, the feedstock's flow is set to 300 t/h. In our approach, the inlet flowrate was fixed and the outlet flow rate values depend on the selected processes.

Many chemical compounds of wood do not belong mainly to the Aspen Plus® databases, and then we need to specify the missing physico-chemical properties (molar mass, atomic structure, density, critical properties, vaporization temperature and enthalpy, etc). A specific compound database was created based on experimental data extracted from literature. Nevertheless, literature does not inform all properties, and then the missing coefficients are calculated through parametric estimations using experimental and theoretical data.

2.1.2.2. Step 4—pretreatments. The objective of pretreatment is to separate different components of the feedstock in shorter molecules and convert them into sugars for the fermentation.

Because wood is mainly composed by cellulose, xylan, galactan, arabinan and mannan, the easiest sugars to create are glucose, xylose, arabinose, galactose and mannose, which can be consumed by the selected bacterium. Several alternatives exist, e.g. physical, chemical or thermal operations. Each type of pretreatment operates with different operating conditions: temperature, pressure, concentration, catalyzer, residence time, yields, losses and degradation of components. The pretreatment was strongly dependent of a lot on the feedstock nature and composition: the lignocellulosic feedstock must be milled and treated to separate lignin from sugars.

This treatment can be physical (e.g. pyrolysis), physico-chemical (e.g. steam explosion, liquid hot water (LHW) and ammonia fiber explosion (AFEX)), chemical (e.g. organosolv, ozonolysis and alkaline), biological (e.g. biological oxidation) or combination of pretreatments. The characteristics of pretreatments are detailed in Table 4.

According to the previous table, the steam explosion is the most interesting pretreatment because it presents high performances, operational simplicity, cost-effectiveness and it can operate with several essence of wood despite the creation of byproducts (acetic acid, furfural and hydroxymethylfurfural). Moreover, it is possible to limit energy consumption by burning the degraded lignin to produce energy. In this study, for this pretreatment the operating conditions are established relaying on the study of Stenberg et al. [41]: the temperature is set at 210 °C, the residence time at 5.5 min and the acid concentration at 3.5%w/w DM.

2.1.2.3. Step 5—hydrolysis. After the pretreatment, a large amount of the decomposed feedstock was not converted into sugar. Then, hydrolysis allowed finishing the conversion, especially for the hexoses. It exists two main types: enzymatic hydrolysis and acid hydrolysis. The enzymatic hydrolysis worked with soft operating conditions and do not produce byproducts but the reaction yields are average and the hydrolysis medium is much diluted. The acid hydrolysis presented higher yields and lower operating time but operates with hard operating conditions. Unfortunately, it also pro-

Table 4
Characteristics of pretreatments [39,40].

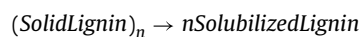
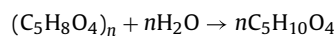
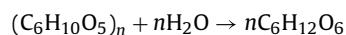
Pretreatment	Advantages	Drawbacks
Alkaline	<ul style="list-style-type: none"> • Effective hemicellulose solubilization • Low generation of toxic compounds 	<ul style="list-style-type: none"> • High degradation of lignin • Requires alkali removal
Organosolv	<ul style="list-style-type: none"> • Effective hemicellulose solubilization • Low generation of toxic compounds 	<ul style="list-style-type: none"> • High cost • Solvents need to be drained and recycled
Ozonolysis	<ul style="list-style-type: none"> • Low generation of toxic compounds • Reduce lignin content 	<ul style="list-style-type: none"> • High cost of large amount of ozone needed
LHW	<ul style="list-style-type: none"> • Requires no catalyst • Low-cost reactor • Low generation of toxic compounds • Effective hemicellulose solubilization 	<ul style="list-style-type: none"> • High water demanding • High energy consumption • Low-solids processing
AFEX	<ul style="list-style-type: none"> • Low generation of toxic compounds • Increases accessible surface area • Low formation of inhibitors 	<ul style="list-style-type: none"> • Not efficient for raw materials with high lignin content • High cost of large amount of ammonia • High degradation of lignin
Steam explosion	<ul style="list-style-type: none"> • Effective hemicellulose solubilization • Cost-effective • Higher yield of cellulose and hemicellulose in the two-step method • Operational simplicity • Efficient on wood 	<ul style="list-style-type: none"> • High formation of toxic compounds • Partial hemicellulose degradation
Biological	<ul style="list-style-type: none"> • Low generation of toxic compounds • Low energy consumption 	<ul style="list-style-type: none"> • Requires long incubation times • Requires careful control of growth conditions
Pyrolysis	<ul style="list-style-type: none"> • Produces gas and liquid products 	<ul style="list-style-type: none"> • High temperature • Ash production

duces byproducts and leads to a substantial impact on environment [42].

The enzymatic hydrolysis is retained because it uses soft operating conditions: aqueous medium, temperature lower than 50 °C and atmospheric pressure. Furthermore, it is a very few polluting process because the use of enzymes limits the production of polluting molecules like acids. Currently, the enzymatic hydrolysis is considered as the most ecological hydrolysis because enzymes are used as catalyzer instead of chemical compounds. However, the conversion performances depend a lot on the enzymatic cocktail which is defined by the used enzymes, their concentration in the mixture and the ratio between the quantity of cocktail and the quantity of feedstock [43]. But the best enzymatic cocktails propose performances in the same order of magnitude that the chemical catalyzers.

For the process modelling, the operating conditions of the enzymatic hydrolysis (40 °C and 0.25 g of enzymes by g of solid) have been tested by Stenberg et al. [41]. We underlined that a step of detoxification with active charcoal follows the hydrolysis in order to remove impurities that can disrupt the fermentation such as furfural or HMF. The active charcoal is regenerated in a furnace, thus this detoxification-regeneration step is considered in our study.

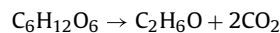
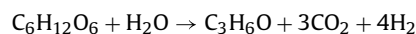
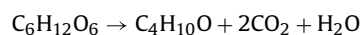
2.1.2.4. Step 6—kinetic of solubilization. The hydrolysis of cellulose and hemicellulose are represented by the following reactions [44]:



The hydrolysis is possible thanks to the action of enzymes. The combination of cellulases like cellobiase, endoglucanase and β -glucosidase allows converting the different types of molecules composing cellulose and hemicellulose.

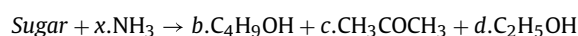
2.1.3. Step 7—kinetics and operating conditions of the ABE fermentation

After the simulation of the pretreatment step, the methodology focuses on the modelling of the fermentation. The ABE fermentation is an anaerobic one, described by the following simplified reactions [30]:



In fact, metabolic pathways in *C. acetobutylicum* are very complex [27]: around twenty reactions and numerous reactive intermediates. Metabolic pathways are decomposed into two steps: first during the acidogenesis the acids are produced, and then these acids are converted into acetone, *n*-butanol and ethanol during the solventogenesis. The reactions are equilibrated, thus some acids are still present at the end of the fermentation.

To simplify reaction kinetics for the process modelling, a simple and total reaction was proposed [45]. It includes growth of bacteria, production of fermentative gases, and consumption of nitrogen nutriment (NH_3). Similar equations are performed for each sugar in the system (hexoses, $C_6H_{12}O_6$ and pentoses, $C_5H_{10}O_5$):



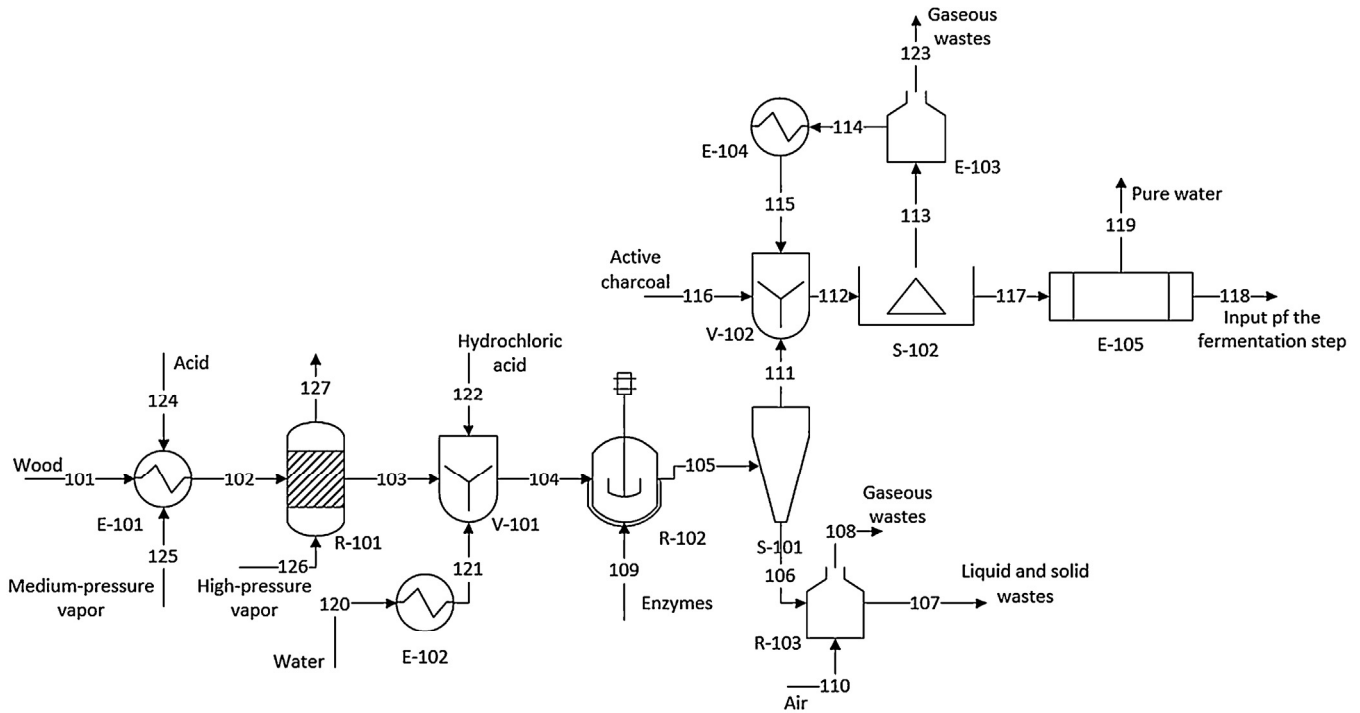
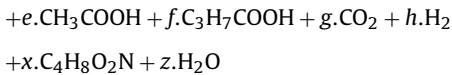


Fig. 2. Flowsheet corresponding to the first step of the biorefinery: steam explosion, enzymatic hydrolysis and detoxification by active charcoal.



Furthermore, stoichiometric coefficients depend on operating conditions of the fermentation. First, we study the concentration and nature of sugars. Experiments proved that the production of ABE is enhanced when the concentration of sugars is increased [46]. Nevertheless, if the concentration of sugars is too high, sugars are not consumed completely. For example, in the experimental work of Monot et al. [46] for a simple batch fermentation with *C. acetobutylicum*, the maximal concentration of sugars for the complete conversion is 40 g/L. Moreover, at low concentration, production of acids is higher than production of solvents, *i.e.* acetone, butanol and ethanol. Thus, concentration should be determined rigorously through a deep literature review in order to reach a complete consumption of sugars and to maximize production of solvents. Many works studied the influence of the nature of sugars on the conversion [29,46–49]. It appears that cellobiose (a sugar composed by two molecules of glucose) presents the highest production of solvents and the lowest production of acids, glucose is the second best substrate and the other sugars have lower rate of reaction and high production of acids.

Next, pH is a very significant operating parameter for the fermentation step as stated by Liew et al. [34] and Lee et al. [27]. They proved that the production of acids and solvents depends on pH: at low pH value (lower than 4.5), the solventogenesis is predominant and production of ABE is high. Conversely, at high pH (between 4.5 and 6.5) the acidogenesis is predominant and the production of acids is high. The dilution rate is also important because it influences the growth of bacteria and ratio between products. According to Liew et al. [34] at low dilution rate, production of solvents and growth of bacteria are higher than at high dilution rate.

The operating conditions of the fermentation have been selected to maximize fermentation efficiency of bacteria. In the case of fermentation with butanol recovery, a higher sugar than for batch fermentation concentration can be used because of the low con-

centration of butanol. According to Kayaalp [29], when the glucose concentration is fixed at 100 g/L and the xylose concentration at 50 g/L, all the glucose and 61% of the xylose are consumed because the reaction rate of pentoses is slower than hexoses. Moreover, according to the simulation of the pretreatment step, 90% of produced sugars are hexoses and the other 10% are pentoses. Thus, in order to consume all sugars, the total concentration of sugars is fixed at 100 g/L in the modelling. Furthermore, the temperature is set to 35 °C and gaseous azote is added to inert the atmosphere.

2.1.4. Thermodynamic background

The thermodynamic background is very important in the process modelling because of the nature of the chemical compounds. Indeed, alcohols and water are very polar compounds leading to a strongly non ideal mixture because of their interactions. For example, the binary water/ethanol leads to an azeotrope and the binary water/*n*-butanol to a heteroazeotrope (an azeotrope with demixtion). Consequently, the thermodynamic background must be rigorous and complete to consider the accurate interactions between molecules. NRTL (Non-Random Two-Liquid) model is selected as thermodynamic model because it includes demixtion and polarity of compounds.

2.1.4.1. Step 8—separation coupled with fermenter. The fermentation broth is composed mainly by water with around 3% w/w of solvents. As a consequence of solvents low composition and of the issues related to thermodynamics, the purification of solvents is difficult, expensive and energy-intensive. To simplify purification, an additional step of separation is necessary to partially withdraw water to limit its quantity before purification.

Furthermore, according to Soni et al. [50], butanol is an inhibitor during the fermentation because it increases the viscosity of the fermentation broth. However, bacteria are very vulnerable to viscosity, *i.e.* their death rate increases at high viscosity. To maintain a low viscosity, several alternatives were considered, but continuous fermentation technologies like *in-situ* recovery of butanol is the most promising one because it does not include negative side

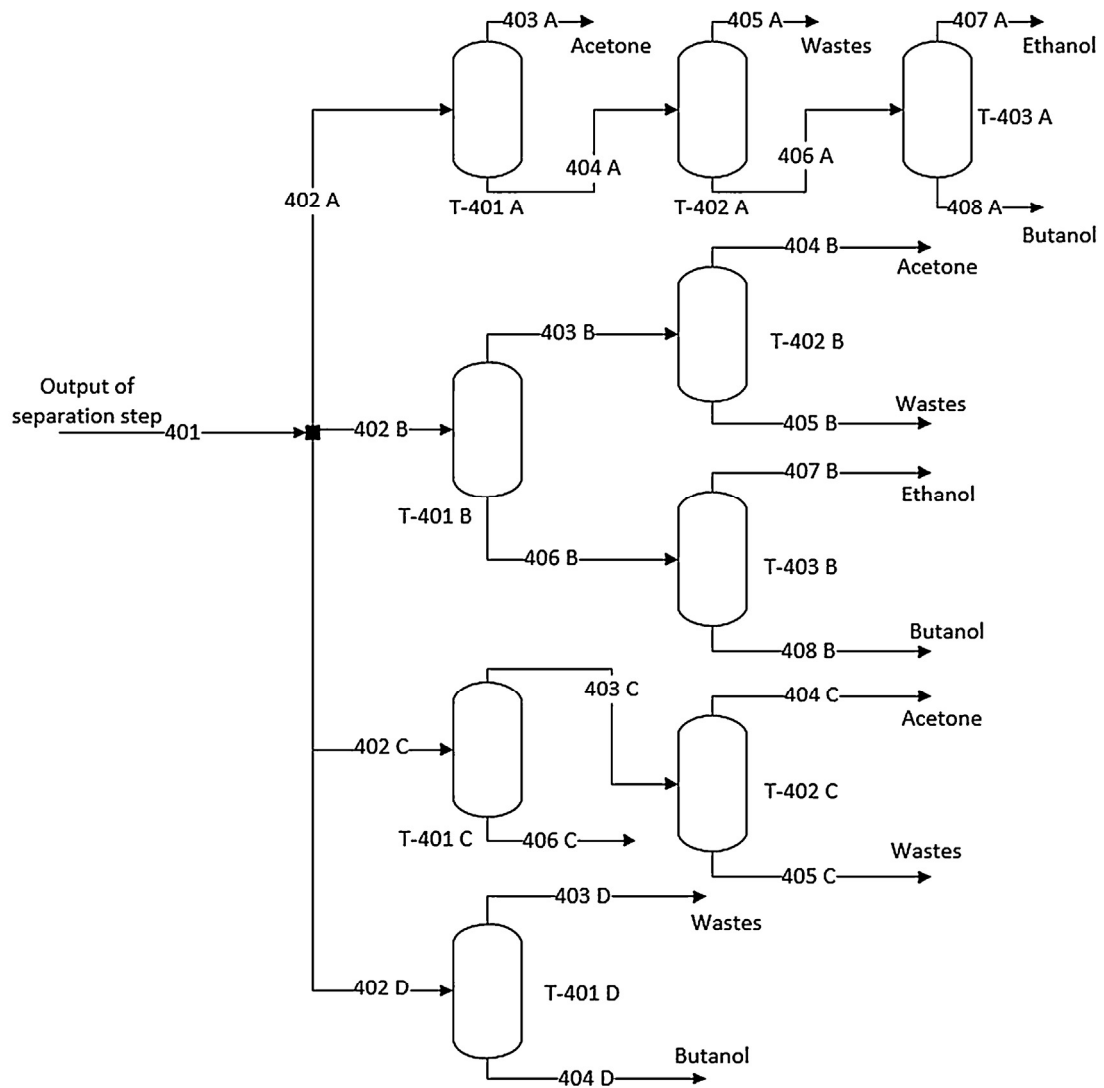


Fig. 3. Superstructure of the 4 purification alternatives.

Table 5
Comparison of *in-situ* separations for the ABE fermentation.

Separation	Advantages	Drawbacks	References
Gas stripping	• No cell damages • Operational simplicity • High flowrates	• High energy consumption • Low selectivity	[7,31,51–54]
Pervaporation	• No cell damages • Low energy-consuming	• Fouling	[29,31,51–53]
Liquid-liquid extraction	• High selectivity • Low energy-consuming • High flowrates	• Possible cell damages (toxicity)	[31,52,53,55]
Adsorption	• No cell damages	• Fouling • No operational simplicity • Low flowrates	[31,51–53,56]
Perstraction	• No cell damages • High selectivity	• Fouling • Low flowrates	[52,53,55,57]

effects on the bacteria's functioning. The *in-situ* recovery of butanol consists in removing continuously butanol from the fermentation broth to limit the inhibition of butanol. Several *in-situ* separations exist and a comparison is drawn in Table 5.

According to Huang et al. [51], pervaporation and liquid-liquid extraction present the most energy-efficient approaches for the removal of butanol from the fermentation broth. On the other hand, gas stripping permits to reach high performances [7]. As a consequence, in this study, we will focus on these three separation technologies. We underline that in the process modelling, the *in-situ* separation has an effect on fermentation thanks to retroaction. Indeed, the performances of the fermentation are improved,

i.e. higher flowrate, increased yields of fermentation, and higher production.

The gas stripping is inserted at the top of the fermenter. During this specific separation, a part of the acetone, ethanol, butanol, water and fermentation gas mixture is condensed and the other part is recycled to the fermenter. The temperature of the condenser, *i.e.* 5 °C, is calculated thanks to a sensitivity analysis determining a good compromise between the recuperation of bioproducts and the concentration of water in the output stream. Indeed, gas stripping is an efficient separation but with a low selectivity, and consequently the output stream contains a large amount of water.

Currently, there is any module of pervaporation available in the commercial version of Aspen Plus8.6®. As a consequence, we have

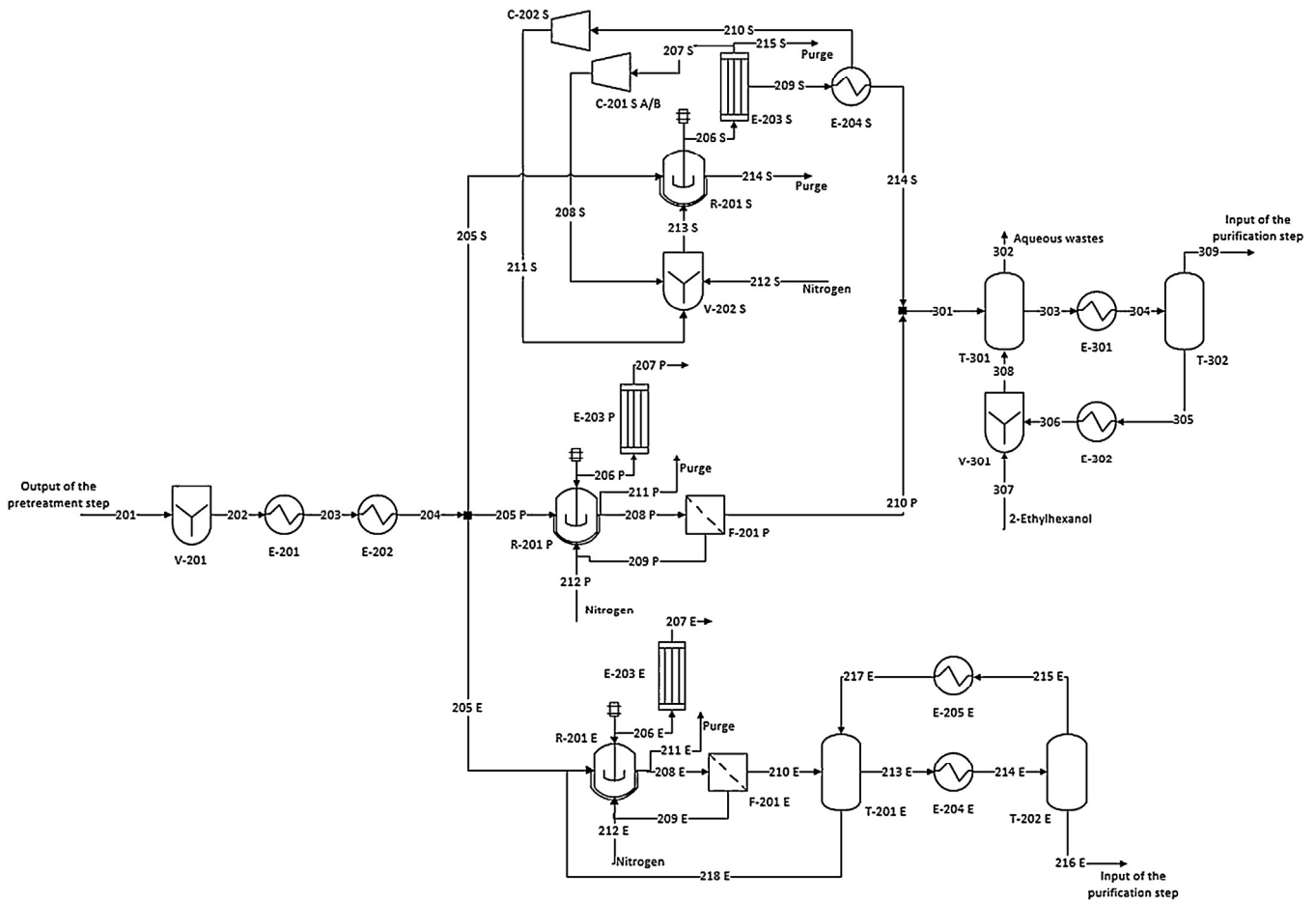


Fig. 4. Superstructure of the coupling fermentation/butanol recovery scenarios.

implemented our own model for the pervaporation unit operation based on a specific separator. The concentrations of acetone, butanol and ethanol in the permeate are calculated with constraints using the separation factors related to water extracted, given by Kayaalp [29]: 22.7 for acetone, 13.7 for butanol and 5.9 for ethanol. The concentration of water in permeate is determined thanks to a sensitivity analysis determining a good compromise between the recuperation of bioproducts and the concentration of water in the output stream.

The selected solvent for the liquid-liquid extraction is mesitylene (1,3,5-trimethylbenzene -CAS number 108-67-8). Binary coefficients (Table 6) and operating conditions (temperature at 35 °C) are either extracted from the work of Krämer [58] or calculated by parametric estimation. The use of liquid-liquid extraction also entails the use of a distillation column for the regeneration of mesitylene to limit input of fresh mesitylene, since this chemical compound is expensive. Moreover, it is necessary to include a microfiltration stage before the extraction column because mesitylene is toxic for the bacteria. According to Meyer and Papoutsakis [59], the recycle ratio (the flow rate of the cell-free product stream divided by the feed stream) of the microfiltration is set to 30% w/w with a dilution rate of 0.287 h^{-1} .

2.1.4.2. Step 9—purification. The purification step is the final phase of the process; it aims to obtain the desired products with the required purity. The possible alternatives differ by the sequence of purification of products and the purification of byproducts. As butanol is the targeted bio-product, all alternatives contain the purification of butanol but only some of them include the purification

of byproducts whereas other alternatives consider byproducts as waste. Usually, the purification consists in a train of distillation columns [9,20,23]. Alternatives are defined according to classical heuristics in process design and thermodynamic problems. For example, in some cases, a supplementary column would be needed to offset the presence of an azeotrope because it behaves like a pseudo-component.

The operating conditions of the columns (reflux, massflows of outputs, etc.) are determined regarding the quality and quantity desired of bioproducts. Moreover, the distillation columns are designed through sensitivity analysis to determine good temperature and concentration profiles.

2.2. Optimal design

The optimal design of the biorefinery is determined by a decision support tool based on the profitability, efficiency and sustainability. The tool analyzes the different alternatives of the superstructure through an economic evaluation, utilities consumption and sustainability. It produces as result different optimal process for each individual objective. Then, the best compromise is considered as the selected process for the biorefinery.

2.2.1. Economical study

Thanks to accurate results from the process simulation, the model includes the economic evaluation of the feasible processes. The aim of the economic evaluation was to determine the selling price of biobutanol for a payback period of 3 years but also the important costs of the project during the biorefinery's life: invest-

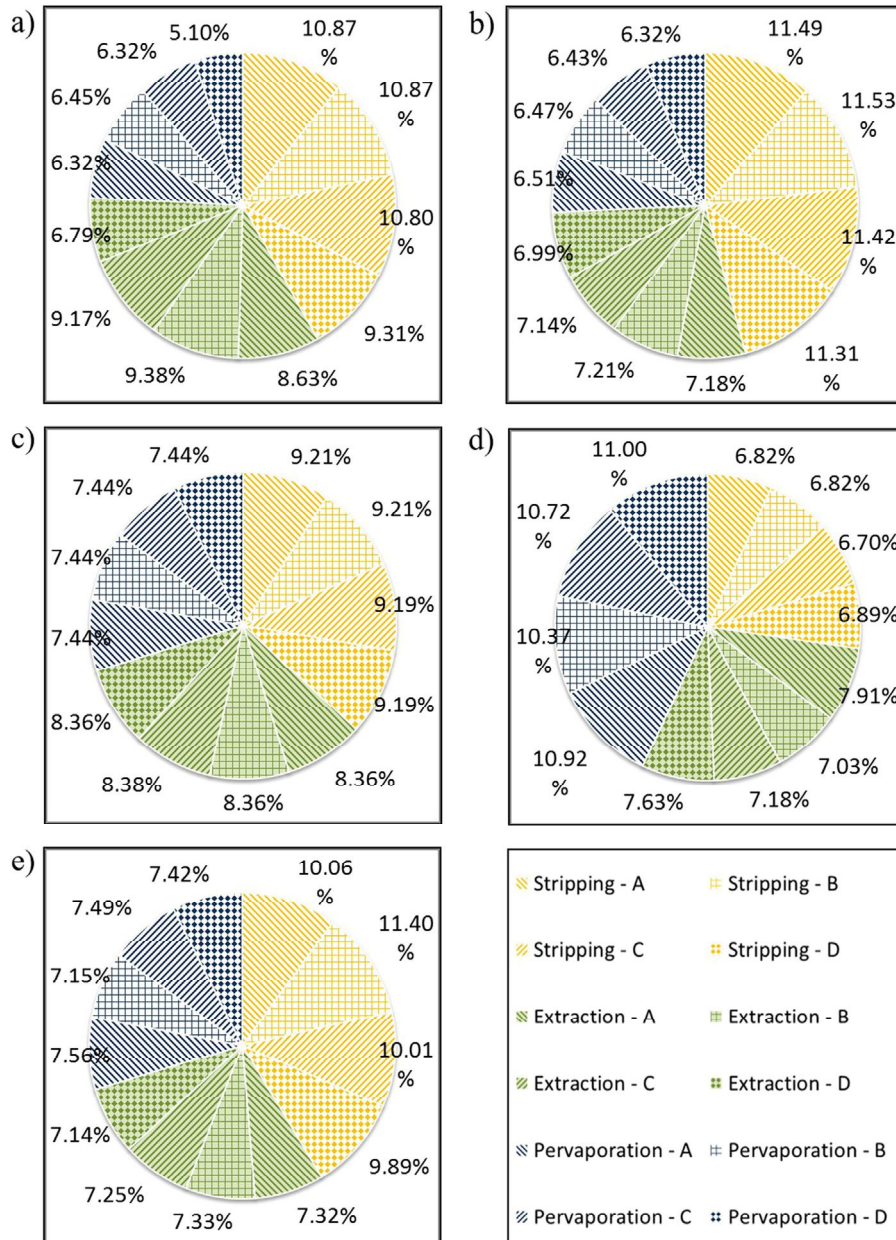


Fig. 5. Comparison of economic and production results for each scenario. a) Acetone-butanol-ethanol production. b) Investment cost. c) Operating cost. d) Butanol selling price. e) Cumulative cash flow.

Table 6
Additional NRTL binary coefficients with mesitylene.

Component i	Water	Butanol	Acetone	Ethanol	Butyric acid	Acetic acid
Component j	Mesitylene	Mesitylene	Mesitylene	Mesitylene	Mesitylene	Mesitylene
Temperature unit	K	K	K	K	K	K
A_{ij}	10.2521	0	0	0	0	0
A_{ji}	-3.7264	0	0	0	0	0
B_{ij}	-66.0366	111.1573	400.1573	737.4539	-28.2385	523.3994
B_{ji}	2542.7793	311.6294	-82.1904	-80.1954	604.0964	485.0802
C_{ij}	0.2000	0.2000	0.3660	0.0770	0.2492	0.5123

ment, operating costs, sales, cash flow, etc. Moreover, the payback time and interest rate represent the risk of the project. Thus, in this study, we fixed the payback time to 3 years in order to simulate bank as a venture capital because no biorefinery exist in France in the present.

This study is carried on with Aspen Process Economic Analyzer[®], where the model encompasses taxes and depreciation. For all the

processes in the superstructure, the calculations were run with the following hypotheses:

- The project duration is 15 years.
- The costs of raw materials are constant through the project lifetime.

- The prices of byproducts are constant through the project lifetime: 1.1 \$/kg for acetone and 0.55 \$/kg for ethanol.
- The liquid waste treatment costs is fixed at 1 \$/m³.

2.2.2. Environmental study

The purpose of the environmental study is to assess the influence of the biorefinery on the environment. This evaluation is relevant in the current context of industrial ecology because chemical enterprises look for a sustainable production.

Many methods based on impact factors exist, but in this study, we retain the impact factors-based method Impact 2002+. This approach combines 14 midpoint categories (expressed in kg-equivalents of a substance compared to a reference substance) and 4 damage categories. A midpoint indicator characterizes the elementary flows and other environmental interventions that contribute to the same impact. In the Impact 2002+ method, the midpoint indicators are the human toxicity, the respiratory effects, the ionizing radiation, the ozone layer depletion, the photochemical oxidation, the aquatic ecotoxicity, the terrestrial ecotoxicity, the terrestrial acidification, the aquatic acidification, the aquatic eutrophication, the land occupation, the global warming, the non-renewable energy and the mineral extraction. Moreover, a damage indicator is the simplified model of a much more complex reality giving only a coarse approximation to the quality status of the substance. The method includes the calculation of human health, ecosystem quality, climate change and resources impacts. Since units of the different impacts are not the same, the method considers the normalization of the factors in Point (noted Pt). It consists on calculating the ratio of the impact per unit of emission divided by the total impact of all substances of the specific category for which characterization factors exist, per person per year.

The calculations are made on the software SimaPro[®] which uses specific databases for the LCA method. The model takes only into account raw materials, utilities consumption, energy consumption, products, wastes and emissions. The chosen boundary of the life cycle assessment concerns activities from the extraction of raw materials (from earth, petroleum and minerals or many materials produced in agriculture e.g. wood) to the end of the ABE production. This boundary is chosen since the study compares the relative life cycle contributions, *i.e.* the method determines the environmental impact to produce one kilogram of ABE. As a consequence, this approach is a cradle to gate study. In addition, the product end of life was not considered, and the comparison is carried between the petrochemical and bio-based ways for the three products. The inputs data for the calculation in SimaPro[®] are presented in the supplementary material.

2.2.3. Energy integration

A large amount of energy is necessary in the biorefinery due to the huge water flowrate in the process that has been estimated to be comprised as 100–500 times higher (in mass) when compared to the production of ABE (especially in the pretreatment step). Thus, energy integration is essential to restrain utilities consumption and to determine the real design of the heat exchanger network. The methodology of the energy integration is not detailed in this study.

3. Results and discussion

3.1. Optimal purification alternative

According to Table 7 and results from the process simulation, the efficiency of pretreatment and hydrolysis (Fig. 2) is only around 31% w/w related on the whole feedstock, but the lignin cannot be converted into substrates for the fermentation. Consequently,

Table 7

Several inputs and outputs of the pretreatment and hydrolysis.

Flow	Mass flows (t/h)
Wood (Fermentable materials)	300 (140)
Enzymes	40
Active charcoal	65
Medium-pressure steam	48
High-pressure steam	714
Input of fermentation (Sugars)	939 (93)

Table 8

Results of the economic and environmental evaluations and productions of scenarios for gas stripping as separation. The environmental impacts are estimated for the production of 1 kg of acetone-butanol-ethanol.

Purification scenario	A	B	C	D
Butanol production (kt/y)	135	136	137	137
Acetone Production (kt/y)	22	22	22	0
Ethanol production (kt/y)	3	2	0	0
Investment cost (MM\$)	309	310	307	304
Operating costs (MM\$/y)	430	430	429	429
Raw materials cost (MM\$/y)	282	282	282	282
Utilities and electricity cost (MM\$/y)	106	106	106	106
Sales (MM\$/y)	753	761	751	745
Butanol price (\$/kg)	5.10	5.10	5.01	5.15
Cumulative cashflow (MM\$)	5289	5458	5264	5188
Environmental impact (mPt/kg of ABE)	28.82	28.21	28.84	33.59

the efficiency increases to 70%w/w compared to the fermentable materials of the feedstock.

Therefore, the losses of fermentable sugars during the first step of the biorefinery are low. Furthermore, the fact that the steam explosion and the detoxification are very energy-consuming unit operations is to be highlighted: the detoxification furnace is the most energy-consuming operation with a total consumption of 837 GJ/h; on the other hand, the steam explosion needs a lot of steam to break down the polymers which compose the wood. Therefore, the previously degraded lignin during pretreatment is burned in a boiler to produce the energy required in order to decrease their energy and utilities consumption. According to the simulation, thanks to lignin valorization, we can reach an energy production of 1335 GJ/h.

Moreover, due to the high amount of steam necessary for the steam explosion, the input flowrate of the fermentation is considerable and composed mainly by water. Thus, the flowrate is divided into 6 similar streams which feed six fermenters in parallel in order to maintain the production if one fermenter is contaminated, to simplify the mixing in the fermenters and to improve process control. Furthermore, this division allows also to limit the size of unit operations in the pretreatment and purification steps of the process.

The optimal purification was studied with gas stripping fixed as the separation unit. From the seven studied alternatives, the four most economically promising ones (based on the butanol selling prices), illustrated in Fig. 3, were examined and compared. Alternative A consists in purifying acetone in the first column, and then in distilling ethanol and butanol. In alternative B, a distillation column separates the azeotropic mixture and acetone from ethanol and butanol, and then two distillation columns purify the products. Alternative C is made up only by the butanol and then acetone distillation columns. Finally, in alternative D, only butanol is distilled. Finally, it is concluded that the purification alternative B was the optimal purification alternative due to the higher cumulative cash flow, a low biobutanol selling price, the highest production and the lowest environmental impact. These results are summarized in Table 8.

Similar studies with pervaporation and liquid-liquid extraction instead of gas stripping were conducted with the four previ-

Table 9

Results of the economic and environmental evaluations and productions of scenarios for liquid-liquid extraction as separation. The environmental impacts are estimated for the production of 1 kg of acetone-butanol-ethanol.

Purification scenario	A	B	C	D
Butanol production (kt/y)	91	102	100	100
Acetone Production (kt/y)	34	34	35	0
Ethanol production (kt/y)	2	2	0	0
Investment cost (MM\$)	193	194	192	188
Operating costs (MM\$/y)	390	390	391	390
Raw materials cost (MM\$/y)	298	298	298	298
Utilities and electricity cost (MM\$/y)	59	59	59	58
Sales (MM\$/y)	617	618	614	610
Butanol price (\$/kg)	5.92	5.26	5.37	5.71
Cumulative cashflow (MM\$)	3833	3840	3789	3733
Environmental impact (mPt/kg of ABE)	10.98	10.03	10.32	12.76

Table 10

Results of the economic and environmental evaluations and productions of scenarios for pervaporation as separation. The environmental impacts are estimated for the production of 1 kg of acetone-butanol-ethanol.

Purification scenario	A	B	C	D
Butanol production (kt/y)	74	76	75	75
Acetone Production (kt/y)	18	18	18	0
Ethanol production (kt/y)	1	1	0	0
Investment cost (MM\$)	175	174	173	170
Operating costs (MM\$/y)	438	438	438	437
Raw materials cost (MM\$/y)	347	347	347	347
Utilities and electricity cost (MM\$/y)	55	55	55	54
Sales (MM\$/y)	669	669	666	662
Butanol price (\$/kg)	8.17	8.00	8.02	8.23
Cumulative cashflow (MM\$)	3999	4028	3957	3908
Environmental impact (mPt/kg of ABE)	29.89	29.43	29.91	36.91

ous alternatives for purification. These show that alternative B is also the optimal purification scheme for each type of separation (Tables 9 and 10). This alternative presents the lowest biobutanol selling price, the highest cumulative cash flow and the highest production. This high profitability can be explained by the distillation sequence: the azeotropic mixture and alcohols are separated in the first column. Thus, on the first side, the azeotropes between water and alcohols do not interfere with the purification of alcohols, and on the other side they do not influence the purification of acetone. Therefore, the parameters of columns e.g. the number of theoretical stages is lower and the operating conditions are more standard and less expensive. Furthermore, the size of the downstream following columns is smaller due to the purification of products in two independent columns.

In addition, the environmental impact of alternative B is the lowest one due to three main reasons: first, whatever the scenario is, climate change is the highest environmental impact, *i.e.* the emission of wastes by the biorefinery is considerably higher. Thus, environmental impact of alternative B is lower because it rejects less waste to the environment than the others. Secondly, the method calculates the environmental impact regarding the production of ABE: higher the production is, lower the impact. Since the production of alternative B is higher, its impact is lower. And finally, the last reason originates from the energy integration which is scenario-specific. In other words, depending on the energy integration, the impact related on the extraction, production, utilization and treatment of utilities can be very different.

Besides, we note that the cumulative cash flow of the pervaporation scenario B is not the highest, but it is the economic study with the biobutanol selling price of the scenario C (the second lowest biobutanol selling price for the pervaporation scenario) which permits to reach a cumulative cash flow of 4106 MM\$. Indeed, alternative B has the highest production. Therefore, if we compare alternatives B and C in using the butanol selling price of the alter-

Table 11

Comparison of economic and production results in function of the butanol recovery.

Separation scenario	Liquid-liquid extraction	Stripping	Pervaporation
Butanol production (kt/y)	102	136	76
Acetone Production (kt/y)	34	33	18
Ethanol production (kt/y)	2	2	1
Investment cost (MM\$)	194	310	174
Operating costs (MM\$/y)	390	430	438
Raw materials cost (MM\$/y)	298	282	347
Utilities and electricity cost (MM\$/y)	59	107	55
Sales (MM\$/y)	618	761	669
Butanol price (\$/kg)	5.26	5.10	8.00
Cumulative cashflow (MM\$)	3840	5458	4028
Environmental impact (mPt/kg of ABE)	10.03	28.21	29.43

native C, the sales and the cumulative cash flow of the alternative B are higher.

On the other hand, for each separation alternative, we underline that scenario D represents the lowest economic and production results and the worst environmental impact. Undeniably, the purification of byproducts (acetone and ethanol) decreases the environmental impact due to the reduction of emissions of wastes and maintains a minimum income *via* the production of byproducts. Indeed, the sole production of butanol is hazardous because of possible events of the butanol market. Thus the purification D cannot be selected in spite of its low investment and operating costs.

3.2. Optimal butanol recovery

In this section, the butanol recovery from the fermentation broth is explained and the three separations alternatives are compared to find the most efficient among them. The superstructure which couples fermentation/separation after process modelling is proposed in Fig. 4. The purification scenario B is fixed for each separation.

The comparison between economic results, environmental impacts and productions is detailed in Table 11. Compared to extraction (respectively pervaporation), the alternative with stripping raises the production of butanol by 25% (respectively 44%). Indeed, gases recycling in the stripping alternative increases flowrate and therefore increases the production. Moreover, scenarios with extraction and stripping produce two times more acetone than scenario with pervaporation. Thus, according to the production indicator, stripping is the more efficient butanol recovery system, followed by liquid-liquid extraction and finally pervaporation.

The investment costs of the extraction and pervaporation scenarios are close but the investment cost for stripping scenario is around 30% higher because of the presence of huge and expensive compressors for gases recycling. On the other hand, the operating cost is mainly made up by raw materials cost and energy cost. Operating costs of stripping and pervaporation scenarios are close also, but the energy cost is predominant for the stripping due to the compression stage whereas the raw materials are preponderant for the pervaporation due to the high input of nitrogen in the fermenters. The operating cost of the extraction scenario is around 10% lower when compared to other scenarios. This difference can be explained by the lower operating charges for the alternative with extraction because of the smaller size of the process unit. Indeed, scenarios containing stripping and pervaporation as purification alternatives include a liquid-liquid extraction that removes remaining water before products purifications, whereas in the extraction alternative case this particular unit operation is combined *i.e.* the extraction is coupled with the fermenter.

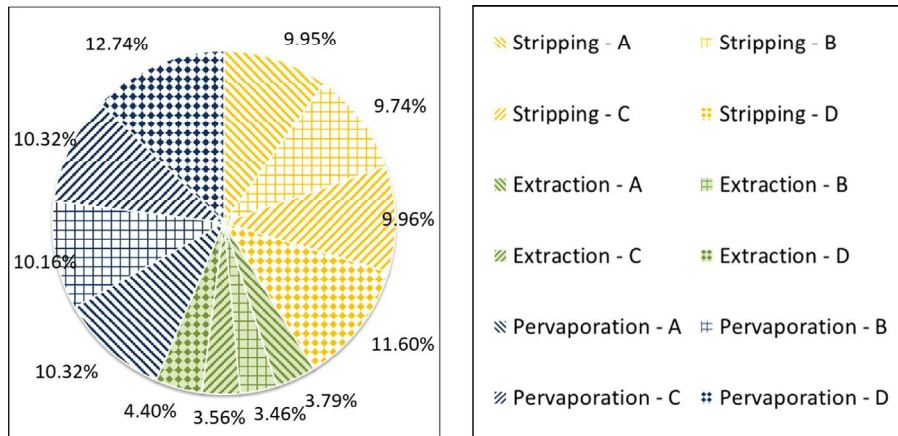


Fig. 6. Comparison of environmental impact for each scenario.

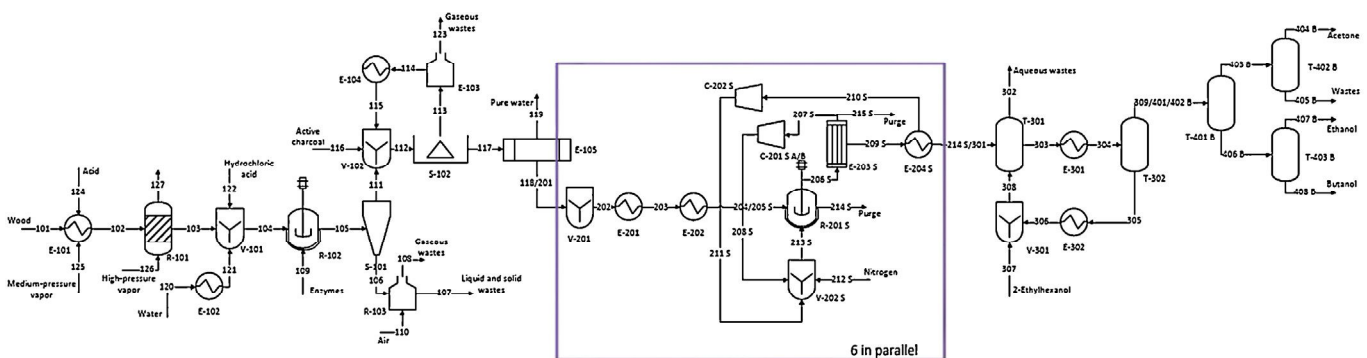


Fig. 7. Flowsheet of the optimal configuration of the biorefinery producing biobutanol.

The stripping scenario presents the lowest biobutanol selling price (5.10 \$/kg) whereas the pervaporation scenario presents a very high price (8.00 \$/kg). We remark that the biobutanol selling price in the extraction scenario is close to the price in the stripping scenario. Finally, the stripping scenario presents the highest cumulative cash flow, which is around 35% higher when compared to other scenarios, because the annual sales are higher due to higher production.

According to the later results, by implementing the stripping scenario a better profitability than extraction and pervaporation scenarios can be reached. Nevertheless, the extraction scenario remains interesting because it presents a low biobutanol selling price. On the first hand, for the pervaporation alternative, fouling of the membrane causes many problems to create a continuous fermentation. On the other hand, selection of a suitable solvent for the *in-situ* extraction is greatly restricted by the direct contact between solvent and cell in the fermenters. Above everything, the organic solvent must be nontoxic to the microorganism. In order to choose the solvent, criteria are: high selectivity with respect to the product, low solubility in the aqueous phase, its density should differ widely forms the broth to ensure separation in the gravity field, low viscosity, large interfacial tension and low tendency to emulsify in the broth, and high chemical stability especially at high temperature during sterilization. Few available solvents respected these criteria.

The environmental study without energy integration shows that environmental impact of the biochemical process is extremely higher than the ecological impact of the petrochemical process, where the major contributor impact are utilities. Indeed, utilities consumption is very large due to the amount of water in the

process. Thus, it is necessary to make the energy integration before the assessment of the environmental impact.

Table 11 shows the comparison between these impacts regarding butanol recovery after energy integration. It can be observed that the impact of stripping and particularly pervaporation are very high (around 30 mPt/kg of products) whereas the impact of liquid-liquid extraction is average (around 10 mPt/kg of products). This difference is originated from the bigger amount of raw materials and waste during the fermentation step, resulting in a higher influence on climate change and resource demand. In fact, the environmental impact measures the ratio between utility flowrate and total production. Moreover, the type of utilities changes for all cases.

Even after energy integration, the environmental impact of the biochemical process remains higher than the impact of the petrochemical process, which is around 1.4 mPt/kg of ABE for each alternative, with a ratio between 7 and 20. In fact, the petrochemical process is currently implemented at an industrial level, thus it is completely optimized whereas the biochemical process is at the early engineering research step. Therefore, it will be necessary to deeply optimize the biochemical process before its implementation at the industrial scale in order to include recycling, improve wastes treatments, etc.

Similar results are found for each fixed purification scenario. The previous results put in evidence that, the stripping scenario is the most interesting one because it is the most efficient, the most profitable and easier to implement industrially. Furthermore, the optimization of the process can be performed to decrease the environmental impact. It is noted also, that the extraction scenario has a high potential due to its relatively low environmental impact and its performances. Thus, it is recommended to improve butanol recov-

ery at the laboratory scale (especially regarding research of green and efficient solvents) before applying again the methodology presented in this study on the ABE production. Finally, the pervaporation scenario is not interesting due to its low economic results, production, ecological performances and considerable problems of fouling.

3.3. Optimal global scenario

In the Sections 3.1 and 3.2, we determined the optimal butanol recovery and the optimal purification sequence. However the optimal global process does not necessarily consists on the combination of both. Through Figs. 5 and 6, all scenarios separation/purification (12 scenarios) are compared. The following equation calculates the percentages presented in the figures:

$$\text{Percentage}(i, j) = \frac{\text{Value}_{i,j}}{\sum_{k=1}^{12} \text{Value}_{k,j}} \times 100, \forall i, j$$

where i, k stand for the alternative and j stand for the variable.

We observe that results can be assembled in function of butanol recovery because results are very similar. Scenarios with pervaporation as separation have the lowest productions (between 0.34% and 5.77%, lower than other separations), the highest butanol selling price (from 2.46% to 4.3%, higher than other scenarios) and low cumulative cash flow (from 2.33% to 4.25%, lower than stripping scenarios) whereas its investment cost and its operating cost are the lowest (from 0.48% to 5.21% and between 0.92% and 1.77% compared to other separations). This low production comes from the low flowrate crossing the membrane. Indeed, higher the recovery of butanol is, higher the water concentration in the permeate, thus it is necessary to establish a compromise between butanol recovery and water concentration in the permeate. On the contrary, in the stripping and extraction alternatives, the output flowrate of the separation are bigger due to more significant recycling and thus an increase in production. Moreover, because of the low production and the high operating cost of pervaporation unit, the butanol selling price must be increased to ensure the financial viability of the biorefinery. The cumulative cash flow for scenarios with extraction and pervaporation are similar whereas the butanol selling price for the pervaporation alternative is higher. Therefore, extraction is more financially viable than pervaporation. Environmental impacts of pervaporation scenarios are similar to impacts of stripping scenarios because of their high utilities and resources consumption but the latter are by 5.8% to 9.3% compared to extraction scenarios due to the higher emission of wastes.

Scenarios with stripping have operating costs similar to extraction scenarios because of the presence of the recycling stream in the separation step. However, the investment cost is higher by an order of magnitude around 4.3% because of gaseous recycling streams that are very expensive due to compressors which maintain constant pressure, whereas the recycling streams in the extraction scenario are in liquid phase. Production of stripping scenarios is larger up to 2% compared to extraction scenarios, and their butanol selling price is lower up to 1.2% and their cumulative cash flow is higher from 2.56% to 4.26%. The difference between productions comes from the different fermentation kinetics used in the two alternatives. According to literature [60], the yields of acids are lower in the presence of stripping in favor on the creation of ABE and bacteria, and thus the production of ABE increases. Furthermore, the higher production allows decreasing the butanol selling price to obtain a financially viable biorefinery. On the other side, the environmental impacts of scenarios with stripping are higher, ranging from 5.3% to 8.1% compared to extraction scenarios due to the higher impact of the life cycle of utilities and electricity used in the stripping alternative. Thus, scenarios with stripping are the

most interesting scenarios regarding the environmental objective. These findings correspond to results determined in Section 3.2.

Moreover, we remark that production and economic performances of the process with alternative B as purification and stripping as recovery are more promising: highest cumulative cash flow, very low biobutanol selling price, very high production of ABE despite the high investment costs and very high energy consumption. Indeed, this process combines advantages of stripping alternative (large recycling and higher yields of ABE that increase production, reduce butanol selling price and improve cumulative cash flow) and the purification alternative B (purification of acetone and ethanol that reduces wastes, standard operating conditions and lower size of unit operations). Nevertheless, it possesses also some drawbacks, namely high energy consumption that leads to an average environmental impact and large and expensive compressors. Therefore, from these analyses, we select this scenario as the best alternative process. On the other hand, the worst scenario is scenario D with pervaporation due to very low economic, production and environmental performances.

We emphasize that the best scenario combines the optimal purification scenario (B) and the optimal separation scenario (stripping) whereas the worst combines the worst purification scenario (D) with the worst butanol recovery (pervaporation). Thus, this study shows that the butanol recovery and the purification step are completely independent. Then, the determination of the global optimal scenario can be the combination of the optimal butanol recovery and the optimal purification scenario.

Finally, the optimal process is summed up in Fig. 7. Concerning energy integration, it is concluded that the optimal heat exchanger network for the selected process is composed by 25 two-stream heat exchangers (and 42 heat exchangers working with utility) and a minimum temperature difference of 5 °C.

4. Conclusion

In this study, the production of *n*-butanol from wood via the acetone-butanol-ethanol fermentation in order to design the optimal process of biorefinery is accomplished successfully. The optimal design of a biorefinery producing butanol is currently problematic due to the lack of complete methodologies taking into account financial viability, sustainability and influence of butanol recovery on the performances of the biorefinery. To tackle these two issues, a multi-scale simulation and optimization tool was created. On one hand, all the necessary data for the rigorous modelling and simulation of the potential ABE processes including the butanol recovery and precise thermodynamic model come from the combination of the molecular, unit operation and process scales. On the other hand, efficiency, profitability and sustainability of the biorefinery are the optimization criteria in order to determine the most profitable process. In this study, we explained step by step our multi-scale methodology for the optimal design of the biorefinery producing butanol and discussed about results.

To create butanol from wood, the methodology focuses on a biorefinery composed by pretreatment, hydrolysis, fermentation, butanol recovery and purification steps and all potential scenarios were studied in details and recapped into a superstructure. The thermodynamic background and the rigorous mass and energy balances of the process modeling and simulation ensured the feasibility of scenarios. In this study, pretreatment, and hydrolysis steps were fixed and whereas the focus was on the coupling between fermentation and butanol recovery and the purification step in order to determine precisely the influence of butanol recovery on the fermentation and the importance to purify the byproducts (acetone and butanol). Then, different criteria, *i.e.* efficiency, profitability and sustainability, were calculated thanks to accurate results of the

simulation. Further from the profitability calculation, the economic study contained the estimation of the theoretical selling price of biobutanol to make profits from the third year. Furthermore, energy integration was performed to optimize the utilities consumption in order to decrease operating cost and environmental impact. Finally, the decision support tool selects the optimal process as a compromise between profitability, efficiency and environmental impact.

According to the decision support tool, stripping was selected as the optimal butanol recovery scenario due to its very high performances whereas the pervaporation presented the worst performances. The liquid-liquid extraction with mesitylene offered average economic results but the best environmental impact. Furthermore, the selected purification scenario consists in the separation of alcohols from acetone, water and the azeotropic mixture, and then other distillation columns purify acetone, ethanol and butanol. Indeed, this scenario presented the most efficient, the most profitable and less polluting results among the four potential purification scenarios. We concluded that the purification of byproducts allows, first, to decrease wastes amount and then the environmental impact, second, to increase incomes and finally to ensure minimum incomes in case of variation of the butanol market. Next, it was found that the optimal global process consists in the combination of both the optimal butanol recovery scenario and the optimal purification scenario. However, we underline that the scenario composed by extraction and the optimal purification scenario offered high potential, so it would be interesting to improve this recovery at the laboratory scale. Finally, the biobutanol price of the optimal biorefinery is four times higher than the price of butanol derived from petrol. We evaluate that our biobutanol will be competitive compared to butanol derived from petrol when the barrel price is four times greater.

The environmental results showed that the bioprocess represents more environmental impacts more than petrochemical process. Thus, it is necessary to improve the optimal process by including more recycling and by applying a process optimization on the parameters of unit operations. Moreover, waste treatments must also be improved to decrease pollution. Furthermore, in future studies the methodology will be applied to the entire process *i.e.* from the pretreatment step until the purification step. Indeed the pretreatment step consumes a large part of the total utilities. Besides, in future work, the methodology will be applied on the design of biorefinery producing other bio-based products in order to evaluate the industrial interest. This can be extended to a portfolio of bioproducts. Another perspective deals with the flexibility of the process in order to take into account the possible variability in the production quantity and on the biomass quality (composition of the feedstock). The flexibility concerns the interval of operations conditions available for each unit operation and for the whole process.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.bej.2016.05.004>.

References

[1] H.T.M. Tran, B. Cheirsilp, B. Hodgson, K. Umsakul, Potential use of *Bacillus subtilis* in a co-culture with *Clostridium butylicum* for acetone-butanol-ethanol production from cassava starch, *Biochem. Eng. J.* 48 (2010) 260–267, <http://dx.doi.org/10.1016/j.bej.2009.11.001>.

[2] M. Kumar, Y. Goyal, A. Sarkar, K. Gayen, Comparative economic assessment of ABE fermentation based on cellulosic and non-cellulosic feedstocks, *Appl. Energy* 93 (2012) 193–204, <http://dx.doi.org/10.1016/j.apenergy.2011.12.079>.

[3] D.C. Rakopoulos, C.D. Rakopoulos, E.G. Giakoumis, Impact of properties of vegetable oil, bio-diesel, ethanol and *n*-butanol on the combustion and emissions of turbocharged HDDI diesel engine operating under steady and transient conditions, *Fuel* 156 (2015) 1–19, <http://dx.doi.org/10.1016/j.fuel.2015.04.021>.

[4] K.R. Szulczyk, Which is a better transportation fuel—butanol or ethanol? *Int. J. Energy Environ.* 1 (2010) 501–512.

[5] P.F.H. Harmsen, M.M. Hackmann, H.L. Bos, Green building blocks for bio-based plastics, *Biofuels Bioprod. Biorefin.* 8 (2014) 306–324, <http://dx.doi.org/10.1002/bbb.1468>.

[6] J. Niemistö, P. Saavalainen, R. Isomäki, T. Kolli, M. Huuhtanen, R.L. Keiski, Biobutanol production from biomass, in: V.K. Gupta, M.G. Tuohy (Eds.), *Biofuel Technol.*, Springer, Berlin Heidelberg, 2013, pp. 443–470, http://link.springer.com/chapter/10.1007/978-3-642-34519-7_17 (accessed 23.06.15).

[7] C. Xue, X.-Q. Zhao, C.-G. Liu, L.-J. Chen, F.-W. Bai, Prospective and development of butanol as an advanced biofuel, *Biotechnol. Adv.* 31 (2013) 1575–1584, <http://dx.doi.org/10.1016/j.biotechadv.2013.08.004>.

[8] V. García, J. Pääkkilä, H. Ojamo, E. Muurinen, R.L. Keiski, Challenges in biobutanol production: how to improve the efficiency? *Renew. Sustain. Energy* 15 (2011) 964–980, <http://dx.doi.org/10.1016/j.rser.2010.11.008>.

[9] Y. Ni, Z. Sun, Recent progress on industrial fermentative production of acetone-butanol-ethanol by *Clostridium acetobutylicum* in China, *Appl. Microbiol. Biotechnol.* 83 (2009) 415–423, <http://dx.doi.org/10.1007/s00253-009-2003-y>.

[10] F. Cherubini, The biorefinery concept: using biomass instead of oil for producing energy and chemicals, *Energy Convers. Manage.* 51 (2010) 1412–1421, <http://dx.doi.org/10.1016/j.enconman.2010.01.015>.

[11] T. Suganya, M. Varman, H.H. Masjuki, S. Renganathan, Macroalgae and microalgae as a potential source for commercial applications along with biofuels production: a biorefinery approach, *Renew. Sustain. Energy Rev.* 55 (2016) 909–941, <http://dx.doi.org/10.1016/j.rser.2015.11.026>.

[12] J.M. Láinez, L. Puigjaner, G.V. Reklaitis, Financial and financial engineering considerations in supply chain and product development pipeline management, *Comput. Chem. Eng.* 33 (2009) 1999–2011, <http://dx.doi.org/10.1016/j.compchemeng.2009.06.025>.

[13] O. Akgul, N. Shah, L.G. Papageorgiou, An optimisation framework for a hybrid first/second generation bioethanol supply chain, *Comput. Chem. Eng.* 42 (2012) 101–114, <http://dx.doi.org/10.1016/j.compchemeng.2012.01.012>.

[14] S.D. Ekşioğlu, A. Acharya, L.E. Leightley, S. Arora, Analyzing the design and management of biomass-to-biorefinery supply chain, *Comput. Ind. Eng.* 57 (2009) 1342–1352, <http://dx.doi.org/10.1016/j.cie.2009.07.003>.

[15] S. Giarola, A. Zamboni, F. Bezzo, Spatially explicit multi-objective optimisation for design and planning of hybrid first and second generation biorefineries, *Comput. Chem. Eng.* 35 (2011) 1782–1797, <http://dx.doi.org/10.1016/j.compchemeng.2011.01.020>.

[16] A.M. El-Halwagi, C. Rosas, J.M. Ponce-Ortega, A. Jiménez-Gutiérrez, M.S. Mannan, M.M. El-Halwagi, Multiobjective optimization of biorefineries with economic and safety objectives, *AIChE J.* 59 (2013) 2427–2434, <http://dx.doi.org/10.1002/aic.14030>.

[17] V. Pham, M. El-Halwagi, Process synthesis and optimization of biorefinery configurations, *AIChE J.* 58 (2012) 1212–1221, <http://dx.doi.org/10.1002/aic.12640>.

[18] J. Moncada, L.G. Matallana, C.A. Cardona, Selection of process pathways for biorefinery design using optimization tools: a colombian case for conversion of sugarcane bagasse to ethanol, poly-3-hydroxybutyrate (PHB), and energy, *Ind. Eng. Chem. Res.* 52 (2013) 4132–4145, <http://dx.doi.org/10.1021/ie3019214>.

[19] N.E. Sammons Jr., W. Yuan, M.R. Eden, B. Aksoy, H.T. Cullinan, Optimal biorefinery product allocation by combining process and economic modeling, *Chem. Eng. Res. Des.* 86 (2008) 800–808, <http://dx.doi.org/10.1016/j.cherd.2008.03.004>.

[20] E. Zondervan, M. Nawaz, A.B. de Haan, J.M. Woodley, R. Gani, Optimal design of a multi-product biorefinery system, *Comput. Chem. Eng.* 35 (2011) 1752–1766, <http://dx.doi.org/10.1016/j.compchemeng.2011.01.042>.

[21] A. Geraili, P. Sharma, J.A. Romagnoli, A modeling framework for design of nonlinear renewable energy systems through integrated simulation modeling and metaheuristic optimization: applications to biorefineries, *Comput. Chem. Eng.* 61 (2014) 102–117, <http://dx.doi.org/10.1016/j.compchemeng.2013.10.005>.

[22] I.E. Grossmann, M. Martín, Energy and water optimization in biofuel plants, *Chin. J. Chem. Eng.* 18 (2010) 914–922, [http://dx.doi.org/10.1016/S1004-9541\(09\)60148-8](http://dx.doi.org/10.1016/S1004-9541(09)60148-8).

[23] L.T. Fan, T. Zhang, J. Liu, P. Seib, F. Friedler, B. Bertok, Price-targeting through iterative flowsheet syntheses in developing novel processing equipment: pervaporation, *Ind. Eng. Chem. Res.* 47 (2008) 1556–1561, <http://dx.doi.org/10.1021/ie070976l>.

[24] M. Stoffers, S. Heitmann, P. Lutze, A. Górak, Integrated processing for the separation of biobutanol. Part A: experimental investigation and process modelling, *Green Process. Synth.* 2 (2013) 101–120, <http://dx.doi.org/10.1515/gps-2013-0009>.

[25] A.B. van der Merwe, H. Cheng, J.F. Görgens, J.H. Knoetze, Comparison of energy efficiency and economics of process designs for biobutanol production

- from sugarcane molasses, *Fuel* 105 (2013) 451–458, <http://dx.doi.org/10.1016/j.fuel.2012.06.058>.
- [26] M. Errico, E. Sanchez Ramirez, J.J. Quiroz-Ramirez, J.G. Segovia-Hernández, B.G. Rong, *Alternative Hybrid Liquid–Liquid and Distillation Sequences for the Biobutanol Separation*, Elsevier, Copenhagen, 2015.
- [27] S.Y. Lee, J.H. Park, S.H. Jang, L.K. Nielsen, J. Kim, K.S. Jung, Fermentative butanol production by *Clostridia*, *Biotechnol. Bioeng.* 101 (2008) 209–228, <http://dx.doi.org/10.1002/bit.22003>.
- [28] B.K. Soni, P. Soucaille, G. Goma, Continuous acetone–butanol fermentation: a global approach for the improvement in the solvent productivity in synthetic medium, *Appl. Microbiol. Biotechnol.* 25 (1987) 317–321, <http://dx.doi.org/10.1007/BF00252540>.
- [29] U. Kayaalp, Two Stage ABE Fermentation with in Situ Pervaporation and High Cell Density, 2013, <http://run.unl.pt/handle/10362/10411> (accessed 23.06.15).
- [30] D. Ballerini, Chapitre 6—La transformation de la biomasse lignocellulosique par voie biochimique, *Biocarburants Etat Lieux Perspect Enjeux Dév.*, Editions TECHNIP, IFP Publication, 2006, pp. 261–306 <http://www.editionstechnip.com/fr/catalogue-detail/2130/biocarburants-les.html>.
- [31] C. Lu, Butanol Production from Lignocellulosic Feedstocks by Acetone–Butanol–Ethanol Fermentation with Integrated Product Recovery, The Ohio State University, 2011, https://etd.ohiolink.edu/ap/1070:NO:10:P10.ACCESION_NUM:osu1306823156 (accessed 23.06.15).
- [32] A.H. Mollah, D.C. Stuckey, The influence of H₂, CO₂ and dilution rate on the continuous fermentation of acetone–butanol, *Appl. Microbiol. Biotechnol.* 37 (1992) 533–538, <http://dx.doi.org/10.1007/BF00240720>.
- [33] J. Formanek, R. Mackie, H.P. Blaschek, Enhanced butanol production by *Clostridium beijerinckii* BA101 grown in semidefined P2 medium containing 6 percent maltodextrin or glucose, *Appl. Environ. Microbiol.* 63 (1997) 2306–2310.
- [34] S.T. Liew, A. Arbakariya, M. Rosfarizan, A.R. Raha, Production of solvent (acetone–butanol–ethanol) in continuous fermentation by *Clostridium saccharobutylicum* DSM 13864 using gelatinised sago starch as a carbon source, *Malays. J. Microbiol.* 2 (2006) 42–50.
- [35] L. Law, Production of Biobutanol from White Grape Pomace by *Clostridium saccharobutylicum* Using Submerged Fermentation, Thesis, Auckland University of Technology, 2010, <http://aut.researchgateway.ac.nz/handle/10292/1017> (accessed 23.06.15).
- [36] Y. Tashiro, K. Takeda, G. Kobayashi, K. Sonomoto, High production of acetone–butanol–ethanol with high cell density culture by cell-recycling and bleeding, *J. Biotechnol.* 120 (2005) 197–206, <http://dx.doi.org/10.1016/j.jbiotec.2005.05.031>.
- [37] Y. Tashiro, K. Takeda, G. Kobayashi, K. Sonomoto, A. Ishizaki, S. Yoshino, High butanol production by *Clostridium saccharoperbutylacetonicum* N1-4 in fed-batch culture with pH-Stat continuous butyric acid and glucose feeding method, *J. Biosci. Bioeng.* 98 (2004) 263–268, [http://dx.doi.org/10.1016/S1389-1723\(04\)00279-8](http://dx.doi.org/10.1016/S1389-1723(04)00279-8).
- [38] C.N. Hamelinck, G. van Hooijdonk, A.P. Faaij, Ethanol from lignocellulosic biomass: techno-economic performance in short-, middle- and long-term, *Biomass Bioenergy* 28 (2005) 384–410, <http://dx.doi.org/10.1016/j.biombioe.2004.09.002>.
- [39] P. Kumar, D.M. Barrett, M.J. Delwiche, P. Stroeve, Methods for pretreatment of lignocellulosic biomass for efficient hydrolysis and biofuel production, *Ind. Eng. Chem. Res.* 48 (2009) 3713–3729, <http://dx.doi.org/10.1021/ie801542g>.
- [40] S. Haghghi Mood, A. Hossein Golfeshan, M. Tabatabaei, G. Salehi Jouzani, G.H. Najafi, M. Gholami, M. Ardjmand, Lignocellulosic biomass to bioethanol, a comprehensive review with a focus on pretreatment, *Renew. Sustain. Energy Rev.* 27 (2013) 77–93, <http://dx.doi.org/10.1016/j.rser.2013.06.033>.
- [41] K. Stenberg, C. Tengborg, M. Galbe, G. Zacchi, Optimisation of steam pretreatment of SO₂-impregnated mixed softwoods for ethanol production, *J. Chem. Technol. Biotechnol.* 71 (1998) 299–308, [http://dx.doi.org/10.1002/\(SICI\)1097-4660\(199804\)71:4<299:AID-JCTB858>3.0.CO;2-Z](http://dx.doi.org/10.1002/(SICI)1097-4660(199804)71:4<299:AID-JCTB858>3.0.CO;2-Z).
- [42] M.J. Taherzadeh, K. Karimi, Enzyme based hydrolysis process for ethanol from lignocellulosic materials: a review, *BioResources* 2 (2007) 707–738, <http://dx.doi.org/10.15376/biores.2.4.707-738>.
- [43] A. Pelletier, K. Li, G. Court, M. Fairbank, M. Frith, Enzymatic pre-treatment of wood chips for energy savings in TMP refining, *J. Sci. Technol. For. Prod. Process.* 4 (2014) 34–49.
- [44] T. López-Arenas, P. Rathi, E. Ramírez-Jiménez, M. Sales-Cruz, Factors affecting the acid pretreatment of lignocellulosic biomass: batch and continuous process, in: SP, G.B. Ferraris (Eds.), *Comput. Aided Chem. Eng.*, Elsevier, 2010, pp. 979–984, <http://www.sciencedirect.com/science/article/pii/S1570794610281646> (accessed 20.11.15).
- [45] L. Yerushalmi, Physiological Aspects of the Acetone–Butanol Fermentation, 1985, http://digitool.library.mcgill.ca/R/?func=dbin-jump-full&object_id=71969&local_base=GEN01-MCG02 (accessed 25.06.15).
- [46] F. Monot, J.-R. Martin, H. Petitdemange, R. Gay, Acetone and butanol production by *Clostridium acetobutylicum* in a synthetic medium, *Appl. Environ. Microbiol.* 44 (1982) 1318–1324.
- [47] M. Mes-Hartree, J.N. Saddler, Butanol production of *Clostridium acetobutylicum* grown on sugars found in hemicellulose hydrolysates, *Biotechnol. Lett.* 4 (1982) 247–252, <http://dx.doi.org/10.1007/BF00132395>.
- [48] W. Morris, Y. Shiyuan, Acetone–butanol fermentation of xylose and sugar mixture, *Biotechnol. Lett.* 7 (1985) 255–260.
- [49] K. Ounine, H. Petitdemange, G. Ravat, R. Gay, Acetone–butanol production from pentoses by *Clostridium acetobutylicum*, *Biotechnol. Lett.* 5 (1983) 605–610, <http://dx.doi.org/10.1007/BF00130841>.
- [50] B.K. Soni, D.K. Das, T.K. Ghose, Inhibitory factors involved in acetone–butanol fermentation by *Clostridium saccharoperbutylacetonicum*, *Curr. Microbiol.* 16 (1987) 61–67, <http://dx.doi.org/10.1007/BF01588173>.
- [51] H.-J. Huang, S. Ramaswamy, Y. Liu, Separation and purification of biobutanol during bioconversion of biomass, *Sep. Purif. Technol.* 132 (2014) 513–540, <http://dx.doi.org/10.1016/j.seppur.2014.06.013>.
- [52] N. Abdehagh, F.H. Tezel, J. Thibault, Separation techniques in butanol production: challenges and developments, *Biomass Bioenergy* 60 (2014) 222–246, <http://dx.doi.org/10.1016/j.biombioe.2013.10.003>.
- [53] W.J. Groot, R.G.J.M. van der Lans, K.C.A.M. Luyben, Technologies for butanol recovery integrated with fermentations, *Process Biochem.* 27 (1992) 61–75, [http://dx.doi.org/10.1016/0032-9592\(92\)80012-R](http://dx.doi.org/10.1016/0032-9592(92)80012-R).
- [54] N. Qureshi, H.P. Blaschek, Recovery of butanol from fermentation broth by gas stripping, *Renew. Energy* 22 (2001) 557–564, [http://dx.doi.org/10.1016/S0960-1481\(00\)00108-7](http://dx.doi.org/10.1016/S0960-1481(00)00108-7).
- [55] W.J. Groot, H.S. Soedjak, P.B. Donck, R.G.J.M. van der Lans, K.C.A.M. Luyben, J.M.K. Timmer, Butanol recovery from fermentations by liquid–liquid extraction and membrane solvent extraction, *Bioprocess Eng.* 5 (1990) 203–216, <http://dx.doi.org/10.1007/BF00376227>.
- [56] N. Qureshi, S. Hughes, I.S. Maddox, M.A. Cotta, Energy-efficient recovery of butanol from model solutions and fermentation broth by adsorption, *Bioprocess Biosyst. Eng.* 27 (2005) 215–222, <http://dx.doi.org/10.1007/s00449-005-0402-8>.
- [57] N. Qureshi, I.S. Maddox, A. Friedl, Application of continuous substrate feeding to the ABE fermentation: relief of product inhibition using extraction, perstraction, stripping, and pervaporation, *Biotechnol. Prog.* 8 (1992) 382–390, <http://dx.doi.org/10.1021/bp00017a002>.
- [58] K. Krämer, Optimization-based Synthesis of Hybrid Separation Processes, 2012 <http://publications.rwth-aachen.de/record/197493/files/4321.pdf>.
- [59] C.L. Meyer, E.T. Papoutsakis, Continuous and biomass recycle fermentations of *Clostridium acetobutylicum*, *Bioprocess Eng.* 4 (1989) 1–10, <http://dx.doi.org/10.1007/BF00612664>.
- [60] W.J. Groot, R.G.J.M. van der Lans, K.C.A.M. Luyben, Batch and continuous butanol fermentations with free cells: integration with product recovery by gas-stripping, *Appl. Microbiol. Biotechnol.* 32 (1989) 305–308, <http://dx.doi.org/10.1007/BF00184979>.