

1 **Economic optimization of *in situ* extraction of inhibitors in acetone-ethanol-butanol (ABE)**
2 **fermentation from lignocellulose**

3 Víctor Hugo Grisales Díaz^{1*} and Gerard Olivar Tost²

4 ¹School of Engineering, Newcastle University, Newcastle upon Tyne NE1 7RU, UK

5 ²Faculty of Engineering and Architecture. Universidad Nacional de Colombia – Sede
6 Manizales, Cra. 27 No. 64-60, Manizales, Colombia.

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8 Author information:

9 Corresponding Author

10 *E-mail: Victor.Grisales-Diaz@newcastle.ac.uk.

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23 **Abstract**

24 The inhibitors produced in the pretreatment (phenolics, furans, and organic acids) as well
25 as in the fermentation (butanol and organic acids) limit acetone, butanol, and ethanol (ABE)
26 production from lignocellulose. To reduce their negative impact on the fermentation, a
27 process involving simultaneous saccharification, ABE fermentation, and detoxification by
28 liquid-liquid extraction was proposed and economically optimized. Although several
29 extractants may be used to reduce butanol toxicity increasing the reactor performance,
30 simultaneous detoxification of inhibitors from pretreatment (IFP) is difficult due to their
31 high boiling point. Hence, the simultaneous detoxification system was evaluated using the
32 biocompatible extractant: oleyl alcohol (boiling point of ~350 °C). Given that oleyl alcohol
33 and IFP have a high boiling point, a heat-integrated distillation system with low-pressure
34 columns was proposed to reduce the energy requirements of the purification of IFP and
35 products from the fermentation. The simulations were performed rigorously in Aspen Plus®
36 and Matlab® at different concentrations of IFP. Although IFP and butyric acid production
37 become feasible ABE production by SSF-E at concentrations of IFP between 13.5 and 30 g/l,
38 the energy requirements were between 1.2- and 2.4-fold higher than that for IFP
39 concentrations of 9 g/l, respectively.

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41 **Keywords:** Hybrid fermentation and separation; detoxification; energy evaluation; liquid-
42 liquid extraction; *in situ* recovery reactor; heat-integrated distillation

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45 **Nomenclature**

46 AA, acetic acid

47 ABE, acetone, butanol, and ethanol

48 BA, butyric acid

49 C_t , solvent cost

50 EP, economic potential

51 FuOL, furfuryl alcohol

52 IFP, inhibitors from pretreatment

53 ISRR, *in situ* recovery reactor

54 LCB, lignocellulose

55 SSF-E, simultaneous fermentation, saccharification, and extraction

56 TIAC, total investment annualized cost

57 TOAC, total operational annualized cost

58 VaN, vanillin

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67 **1. Introduction**

68 Butanol has better properties than ethanol as biofuel and it is an important industrial
69 chemical [1,2]. Biologically, butanol is produced in the acetone, butanol, and ethanol (ABE)
70 fermentation. This was the second fermentation in importance in the world on mid-
71 twentieth century [3]. However, it was not able to compete with petrochemical production
72 [4]. Currently, fluctuations in oil price, diminishing of oil resources, environmental worries,
73 and the good qualities of butanol as biofuel have re-established its production by ABE
74 fermentation in some places of the world (e.g., China and Brazil) [3,5]. Batch fermentations
75 and continuous production by tank-in-series systems are commonly used in industry [6].
76 Distillation has been reported as the conventional method used for ABE recovery in Chinese
77 industry [6]. Although distillation is considered to have a high-energy demand by some
78 researchers [6], Jilin Cathy Industrial Biotech, one of the main butanol producers in China,
79 reports low energy requirements using distillation [6] (6-7 kg-steam/kg-butanol [6] or 8-
80 9.4 MJ fuel/kg ABE [7]). In similar way, a recent academic study of four heat-integrated
81 distillation systems shows low energy requirements too (between 4.7 and 11.5 MJ fuel/kg
82 ABE [7]).

83 Lignocellulose (LCB) is the most abundant renewable resource for ABE production.
84 Due to butanol inhibition, ABE production from detoxified LCB hydrolysates in conventional
85 batch processes is an uneconomical alternative [8]. Given that *in situ* recovery reactors
86 (ISRR) reduces butanol inhibition, ISRR are interesting and intensively investigated in ABE
87 production. These processes include pervaporation, liquid-liquid extraction, adsorption,
88 vacuum evaporation, and gas stripping [9–11]. In addition, a hybrid of gas-stripping and

89 pervaporation system has been recently proposed [12,13]. However, given that these
90 recovery systems represent an additional investment and operative costs, the total
91 annualized costs are not necessarily lower than that of conventional reactors [8]. Hence, an
92 economical optimization is necessary to select the operational conditions [8].

93 Due to the several inhibitors produced in the pretreatment, LCB hydrolysates can be
94 not fed directly in the ISRR by vacuum evaporation or pervaporation without detoxification
95 [8]. The inhibitors from pretreatment (IFP) can be divided into three groups: phenolics,
96 furans, and organic acids. The ratio and concentration of IFP depend on the selected process
97 and the parameters of the pretreatment [14]. For instance, the total concentrations of
98 furans and phenolics using corn stover (35 wt%) and sugarcane bagasse (16.7 wt%) obtained
99 from dilute acid pretreatment were 17 g/l [15] and 21.4 g/l [16], respectively. Phenolic
100 compounds are the most toxic for the microbial strains used in the ABE fermentation. A
101 concentration of 0.5 g/l of ferulic acid entirely inhibits ABE production by *Clostridium*
102 *beijerinckii* BA101 [17]. Similarly, this concentration of ferulic acid decreases the growth of
103 *C. beijerinckii* NCIMB 8052 by 30%, and the final ABE concentration from 14.0 to 11.7 g/l
104 [18]. In comparison, butanol completely inhibits the ABE fermentation only at much higher
105 concentrations, of between 13 and 20 g/l [19–21]

106 The concentrations of IFP may be reduced by washing or other detoxification
107 methods. Although washing only requires water, dilution of substrate concentration
108 increases the total annualized costs (TAC) and reduces the energy efficiency of *in situ*
109 recovery processes for ABE production [8]. Other detoxification methods before

110 fermentation include extraction, adsorption, evaporation, electrodialysis, over-liming,
111 neutralization, steam stripping, enzymatic and microbial treatment [22,23].

112 In this work, we focus on liquid-liquid extraction. In detoxification systems with
113 extraction, solvents of medium boiling point (e.g., decanol (DAL), 232 °C [24]) have been
114 proposed. However, extraction requires a high-boiling solvent because of the high boiling
115 points of furans and phenolics. For example, coumaric and ferulic acid, the primary products
116 of lignin degradation, have boiling points of 316 and 405 °C, respectively. Therefore, the
117 extractant will be obtained at the top of a regeneration column by distillation. Due to the
118 high flow of extractant necessary to recovery IFP at low concentrations, regeneration of
119 extractants with a lower boiling point than that of phenolics by distillation will be difficult.

120 Extractive fermentation is a more attractive option for detoxification than extraction
121 before fermentation, mainly, because increases the performance of the reactor intensifying
122 the process. Additionally, *Clostridium* strains, advantageously, transform these phenolic
123 acids into molecules with a lower boiling point. For instance, *p*-coumaric acid is converted
124 to *p*-hydroxyl-hydrocinnamic acid (285 °C) by reduction to 4-vinylphenol (229 °C) and then
125 4-ethylphenol (218 °C) [14]. Oleyl alcohol (OAL), the most studied extractant for *in situ*
126 extraction, has a boiling point of 357 °C. Therefore, the regeneration of a high-boiling
127 extractant by distillation becomes more feasible (the extractant is obtained at the bottoms).

128 At the best of our knowledge, a scheme of production of ABE, butyric acid (BA),
129 furans and phenolic compounds by liquid-liquid extraction has been not studied in the
130 literature. Process modeling is an important tool to determinate the viability of new
131 processes [25–28]. For these reasons, in this work, a detoxification system with

132 simultaneous saccharification, fermentation, and extraction (SSF-E) (Fig. 1) was simulated
133 and optimized economically. Additionally, a heat-integrated distillation system was
134 simulated and proposed as the purification method to reduce the energy requirements. The
135 cost of selling of IFP (vanillin and furfuryl alcohol) and BA was studied.

136 **2. Material and Methods**

137 *2.1. Thermodynamic model*

138 SSF-E was simulated in both Matlab 2016a[®] and Aspen Plus V9[®]. The process model
139 developed for ISRR by vacuum stripping and pervaporation [8] was adapted to ISRR by
140 liquid-liquid extraction [29]. The production of gases is included in the reactor model. The
141 property method was UNIQUAC [8]. In the detoxification system, OAL was selected as the
142 extractant based on its high boiling point (357°C), biocompatibility, acceptable distribution
143 coefficient (3.8) and high selectivity (~300).

144 Vanillin (VaN) and FuOL were selected as the phenolic and the furan compounds,
145 respectively. VaN was chosen to represent the properties of the phenolic compounds
146 because it has a high boiling point (285 °C). Additionally, solubilized lignin is simulated as
147 VaN [30]. Due to the high conversion rate of furfural (0.15 g/l/h [14]) to furfuryl alcohol
148 (FuOL), total conversion of furfural was assumed. For this reason, FuOL was studied.
149 Interestingly, FuOL is the primary commercial chemical derivative from furfural.

150 Since VaN and FuOL were selected as representative molecules of the two groups of
151 compounds (phenolics and furans, respectively), which involve many different species, their
152 extraction by OAL was simulated with lower distribution coefficients than those measured
153 and reported in the literature at low concentrations [24] (Table 1). This conservative choice

154 takes into account the complex nature of the inhibitors. The distribution coefficients of VaN
155 and FuOL used in this work were 3 (53% of experimental value) and 1 (38.5% of predicted
156 value), respectively. Only VaN and FuOL were extracted in the simulation with a constant
157 distribution coefficient. The temperature of extraction was equal than that of the
158 fermentation (30 °C).

159 *2.2. Kinetic model*

160 The kinetic model of ABE fermentation by *Clostridium saccharoperbutylacetonicum*
161 *N1-1* includes the effect of IFP on growth [8] and is based on the experimental data reported
162 by [31–33]. The metabolic kinetic model included 15 components (glucose, xylose, BA,
163 acetic acid, pyruvate, acetyl-CoA, acetoacetyl-CoA, butyryl-CoA, acetone, butanol, ethanol,
164 active biomass, dead biomass, CO₂ and H₂). The average errors in the predictions of the final
165 concentrations of butanol and acetone of this kinetic model are 3.4 and 8.3%, respectively.
166 The average error prediction of the model for ABE production in the presence of IFP is 8.3%
167 [8]. The inhibition of IFP was included in the kinetic model using exponential inhibition
168 terms on biomass growth. The kinetic model for hydrolysis was proposed by [34]. The
169 kinetic had three reactive components (cellulose, cellobiose and glucose) and the inhibition
170 of xylose on the hydrolysis. The structures of the kinetic models studied in this work are not
171 available in Aspen Plus[®]. Hence, the selection of optimal conditions was performed through
172 a rigorous simulation in Matlab 2016a[®].

173 *2.3. Model process*

174 The operational mode of SSF-E was continuous. SSF-E was simulated in Matlab[®] and
175 Aspen Plus[®]. To find the global conversions (acetone, butanol, ethanol, AA and BA) and the

176 extractant flow required in SSF-E, the algorithm of the simulations performed in this work
177 has three steps. In step one (Fig. 2), the sizing functions of the regeneration system are
178 defined as function of the ratio between the extractant flow required and the ABE produced
179 and VaN recovered [29]. The column diameter, heat consumption and temperatures of the
180 units required for the regeneration of the extractant were determined in a sensitivity
181 analysis carried out in Aspen Plus V9[®]. The correlation coefficients of the sizing units from
182 the sensitivity analysis were higher than 0.993 [29]. In the simultaneous detoxification
183 system, the data from the sensitivity analysis were adjusted to a ratio of extractant/solvent
184 between 12 and 160 kg-OAL/kg-ABE [29].

185 In Matlab[®] (step two, Fig. 2), the *in situ* recovery system was simulated in pseudo-
186 steady-state (the reactor is simulated in a dynamic state and the extraction unit in
187 continuous, [29,35]). Although SSF-E was studied only in continuous operation, the dynamic
188 effect on the reactor performance by the starting of the fermentation and the total
189 fermentation time were included in the simulations. The fermentation time of SSF-E was
190 limited to 500 h [36]. The reactor started in batch and continuous separation and operation
191 were only initiated after 20 h [36]. The initial concentration of cellulose in the reactor and
192 cellulose concentration from pretreatment in the continuous feeding were 20 and 120 g/l
193 in all cases, respectively [8]. The volume of reactors was 1000 m³. The working volume
194 (aqueous and organic phase) of each reactor was 80% (v/v). The total flow of LCB was 25000
195 kg-dry-LCB/h. In this work, the word “substrate” is used to refer to the sum of cellulose and
196 xylose. The feeding ratio of cellulose/lignin/xylose was fixed to 2/1.5/1 [8].

197 Enzyme load, residence times, and solvent flow of SSF-E were selected from the
198 maximization of the economic potential (EP, MM USD/year) given by:

$$EP = \sum F_{ABE_i} \cdot C_i \cdot t_a - (TOAC + TIAC) \quad (1)$$

199 where TOAC is the total operation annualized costs (MM USD/year), TIAC is the total
200 annualized investment cost (MM USD/year), F_{ABE} is the product flow recovered, and t_a is the
201 annual time of operation (8150 h). The time of return of inversion was three years.

202 In the optimization, the reactor, exchanger, extractant and regeneration column
203 costs were included in the estimation of TIAC, while steam, cooling water, enzyme, and
204 substrate costs were included in the estimated of TOAC. The economic functions in the
205 process optimization were reported by [8]. To ensure a global maximum, the optimization
206 was performed using the function 'fminsearch' of Matlab® and several random initial
207 estimates. The selling prices (\$) of butanol, acetone, ethanol and BA were 1, 0.7, 0.8 and 2
208 \$/kg, respectively [37]. OAL had a cost of 4.3 \$/kg [37], respectively. The enzyme cost was
209 4.24 \$/kg. The cost of low pressure steam, medium pressure steam and high pressure steam
210 were 2.18 \$/ton-steam (3 bar), 7.9 \$/ton-steam (30 bar) and 11.8 \$/ton-steam (105 bar)
211 [10], respectively. Cooling water and electricity costs were 0.06 \$/ton-water and 0.1 \$/kWh,
212 respectively.

213 The initial investment of the extractant is the multiplication of extractant flow (kg/h),
214 extractant cost (USD/kg) and its residence time (h) in the units involved in the extraction
215 (reactor, regeneration columns, heat exchangers, pipelines, i.a.). Low residence times
216 means that the volume occupied by the extractant in the reactor will be low. Hence, the
217 organic phase will be technically difficult to separate from the aqueous phase and the

218 efficiency of the extraction may be reduced. In this work, a conservative residence time of
219 4 h was assumed. In perspective, in this work depending on the flow of extractant, the
220 volume of the organic phase with this ratio was between 4 and 21% of the volume of
221 reactor. In future work, a model including mass transfer coefficients or non-equilibrium
222 models will be necessary for the calculation of the extractant flow and initial extractant
223 investment.

224 Once the optimal conditions were found in Matlab[®], simulations of the regeneration
225 and final purification system (section 2.4, Fig. 3) in Aspen Plus[®] were performed to obtain
226 the total energy requirements and the total separation costs. In addition, extractant losses
227 in the vinasses were obtained and included in the TOAC. The configuration of the SSF-E was
228 analogous to that performed in Matlab[®], however, the reactor was a stoichiometric reactor
229 (Rstoic). The conversions and extractant flow are provided by the results of the optimization
230 performed in Matlab[®]. In this way, the simulation in Aspen Plus[®] is run with the optimal
231 performance of the reactor to calculate the energy requirements and the total recovery
232 costs of SSF-E. The energy analysis was performed in terms of fuel requirements [10,38]. In
233 the energy evaluation, the fuel requirement was estimated with an efficiency for the
234 production of low, medium and high steam pressure of 0.9, 0.85 and 0.8, respectively. The
235 efficiency of electricity production was 0.33.

236 2.4. Distillation system

237 In the economic analysis, the costs to recover ABE from the gas streams is calculated.
238 Non-condensables (CO₂ and H₂) were fed to an absorber column (10 trays and 1 atm) to
239 recover the carried ABE. A water flow of 10000 kg/h was fed at the top of the column to

240 recover ABE from the gases. The liquid aqueous stream from stripping is mixed with the
241 aqueous stream from the reactor. The distillation systems proposed in this work were
242 designed to obtain butanol, acetone, and ethanol at 99.7, 99.5, and 90.0 wt% [7],
243 respectively. Without inhibitors in the prehydrolysates, BA was obtained at 99.7 wt% in SSF-
244 E. The ABE recovery of the total separation system was >0.98 [7].

245 The extractant unrecovered at the top of regeneration column (column 1) was fixed
246 at 1000 kg OAL/h, Fig. 3. This was proposed to improve the heat integration (the
247 temperature of condensation is higher than 136 °C) and the selectivity on the decanter (D1)
248 between the columns 2 and 3 (the water content is reduced by OAL). VaN or butanol
249 recovery in the distillation column was fixed at 0.99. The distillation for SSF-E had seven
250 columns (115 stages, Fig. 3): columns 1 (15 stages), 2 (20 stages), 3 (20 stages), 4 (10 stages),
251 5 (20 stages), 6 (and 15 stages) and 7 (15 stages). The total stages were selected to avoid an
252 excess of trays. In perspective, the number of non-ideal stages used in this work (105 stages)
253 to purify ABE, IFP and OAL from water was lower than that of a regular distillation system
254 of five columns to purify only ABE from water (135 ideal stages [39]). The Murphree
255 efficiency was 0.7. The feed stages were selected to minimize the energy requirements of
256 the distillation columns. The aqueous streams from the reactor and decanter to C2 were
257 fed to the stages 4 and 1, respectively. The feeding stages to C3, C6 and C7 were 11, 5 and
258 8, respectively. Whist, the streams to C1, C4 and C5 were fed to the stages 8, 1 and 15,
259 respectively.

260 In the column 2, the residual ABE from the reactor is recovered from the aqueous
261 phase. In the column 3, ethanol and acetone are recovered at the top. In column 5, acetone

262 and ethanol are purified at the top and bottoms, respectively. Whilst, butanol was purified
263 in the column 6. BA was found in a mixture with FuOL, VaN, and OAL at the top of column
264 7. Due to an azeotrope estimated by the simulator between VaN and OAL, OAL was not
265 entirely recovered. It is important to mention that this azeotrope must be confirmed
266 experimentally.

267 The aqueous and organic streams were preheated with the vinasses and recovered
268 extractant, respectively [7]. In heat-integrated distillation, the pressure of the columns is
269 manipulated to apply energy of condensation to the boilers [7,38,40]. To make possible this
270 heat integration, the pressure of columns 2 (0.3 bar), 3 (0.6 bar) and 5 (0.5 bar) was selected
271 to have a boiling temperature around 80 °C. Due to the high boiling temperature of OAL
272 and IFP, the columns 1 (0.1 bar), 4 (0.75 bar), 6 (0.4 bar) and 7 (0.1 bar) were operated to
273 vacuum. However, the condensation temperature of the condenser of the columns 1, 6 and
274 7 still were higher than 90 °C, hence, the steam from the top of this columns was condensed
275 in the boilers of the columns 2, 3 and 5. C4 does not has a condenser. Only when IFP were
276 fed to the reactor (IFP>4.5 g/l), the condenser temperature of boiler 7 was used to provide
277 heat to columns 2, 3 or 5. Simulations were performed with a minimum approach
278 temperature of 10 °C.

279 **3. Results and discussion**

280 The coefficients of partition were found to be dependent on the concentration of
281 the components presents in the reactor and the recovery achieved. For instance, the
282 butanol distribution coefficient using OAL was reduced from 3.9 (simulated) or 3.8
283 (experimental [41]) to 2.7 (IFP=0 g/l). The number of reactors was 8 (1000 m³ each one). In

284 comparison, a conventional batch reactor achieving the same level of production have been
285 reported to need 21 reactors (1000 m³ each one) [7].

286 The TAC of SSF-E (IFP= 0g/l) was 0.81 \$/kg-ABE (Table 2). The cost of enzymes
287 represents between 8.2 and 11% of the TAC (Table 2). The annualized cost of the reactor
288 was between 1.4- and 2.2- fold higher than that of the enzymes. Substrate cost was the
289 most important factor in the economic performance (IFP<18 g/l). For this reason, if the
290 substrate cost is reduced from 0.12 to 0.06 \$/kg-substrate, the EP increased from 6.94 to
291 15.4 MM US\$/year (IFP of 0 g/l). The total cost of extractant regeneration was 58.8% of the
292 TAC of the distillation system (IFP of 0 g/l). Hence, both regeneration and purification costs
293 are important in the economic evaluation of butanol production by SSF-E.

294 The total recovery costs (IFP of 0 g/l) of SSF-E were 0.19 \$/kg ABE. In perspective,
295 the recovery costs required of a process involving a conventional batch reactor and the
296 most economical distillation process, double-effect distillation, are reported between 0.12
297 and 0.16 \$/kg ABE [7]. These recovery costs are between 16% and 37% lower than that of
298 SSF-E. In addition, the energy requirements of the total recovery and purification system
299 were not necessarily lower than that of conventional processes involving distillation (energy
300 requirements between 4.7 and 11.3 MJ fuel/kg ABE [8]). In fact, a conventional reactor
301 system and ABE recovery by vapor compression distillation or a hybrid system of vapor
302 distillation (or stripping)-vapor permeation have been reported recently as the processes
303 with the lowest energy needs for ABE recovery [7,42] (between 4.2 and 7.3 MJ fuel/kg ABE).
304 However, given that the investment of the reactors and enzyme load are reduced using SSF-

305 E, the TAC of the reaction and recovery system of the conventional process reported by [8]
306 (substrate cost: 0.12 \$/kg) are reduced 20% using SSF-E.

307 Without the costs of the final purification system and using a BA selling cost of 2
308 \$/kg, EP of SSF-E was 8.9 MM US\$/year. Including the purification costs, the EP of SSF-E was
309 reduced from 8.9 to 6.94 MM US\$/year. The profit for BA sale was 1.78 MM US\$/year 65%
310 of BA was recovered (IFP of 0 g/l). The kinetic model predicted an increment of the BA yield
311 from 0.010 to 0.047 g/g-substrate increasing the concentrations of IFP from 0 to 30 g/l (Fig.
312 4). Although the recovery of BA may reduce the ABE yield, an increment of ABE yield from
313 0.29 to 0.34 g/g was achieved because the substrate conversion increased with low dilution
314 rates or productivities and higher extractant flows (Fig. 4). Given that butanol is several
315 times less toxic than phenolic and furans, lower productivities in the reactor were achieved
316 mainly because IFP concentration was increased (Table 2). Butanol concentrations were
317 lower than 6 g/l (Table 2); hence, butanol did not achieved inhibitory levels in the reactor.

318 Under optimal conditions, the kinetic model predicted that AA was totally consumed
319 by the process microorganism in all simulations. The extractant used was 58 kg-
320 extractant/kg-butanol (IFP of 0 g/l). The extractant increased from 58 to 305 kg-
321 extractant/kg-butanol with an increase of IFP concentration from 0 to 30 g/l. For this
322 reason, the energy requirements of the regeneration increased in relation to IFP (Fig. 4).

323 The energy integration proposed in this work (minimum temperature approaching
324 of 10 °C) allowed an energy saving of 73% and energy requirements of 10.7 MJ-fuel/kg-ABE
325 (IFP of 0 g/l). These energy requirements were analogous than that achieved by the ISRR by
326 vacuum evaporation [2]. Vacuum evaporation is a preferable choice than pervaporation

327 from an economic and operational points of views [2]. However, both vacuum evaporation
328 and pervaporation were unprofitable for detoxification. In this work, the concentration of
329 substrate was the maximum restricted in all the cases. Hence, detoxification using SSF-E
330 was more economical than washing (an unprofitable way of detoxification with higher
331 performance than vacuum evaporation and pervaporation [8]).

332 The energy and economic performance of the recovery of SSF-E did not reduce
333 inclusive when concentrations of IFP as high as 9 g/l are fed to the reactor. The design
334 specification of SSF-E with a feed of 0 and 9 g/l of IFP are reported in Table 3. The total fuel
335 consumptions with IFP concentrations of 9 and 18 g/l were between 10.2 and 13.9 MJ-
336 fuel/kg-products (including BA, VaN and FuOL as products), respectively. These energy
337 requirements are still between 10% and 30% lower than that reported for a hybrid system
338 of gas stripping and pervaporation (15.8 MJ/kg ABE [12]).

339 The fuel requirement of the regeneration system rose from 12.3 to 24.8 MJ-fuel/kg-
340 product, when the IFP concentration increased from 13.5 to 30 g/l. Hence, an IFP
341 concentration lower than 13.5 g/l can be recommended from the energy and operational
342 perspective (Fig. 4). The substrate was the main factor in the economic performance when
343 the concentration of IFP is lower than 18 g/l. When the concentration of IFP fed to the
344 reactor was higher than 18 g/l the recovery cost was the most important factor in the
345 calculation of the TAC (Table 2).

346 Fig. 5 shows the EP of SSF-E of several selling prices of IFP and BA. BA was
347 fundamental for the economy of the process given its high price (two times higher than that
348 of butanol). For this reason, if the selling price of BA is reduced from 2 \$/kg to 0 \$/kg, the

349 minimum selling price that makes profitable the detoxification of 30 g/l of IFP was 1.7 times
350 higher (Fig. 5). However, the EP of the SSF-E will not be necessarily lower than that without
351 IFP because they have a high selling price too. For example, the market prices of VaN and
352 FuOL are 10.5- and 1.9-fold higher, respectively, than that of butanol [37].

353 The maximum necessary selling price of IFP (BA selling price of 0 \$/kg) to equal the
354 performance of 0 g/l of IFP and the current cost of BA was lower than that of the market
355 price of FuOL (1.9 \$/kg). In perspective, gas stripping [43], vacuum evaporation and
356 pervaporation [8] are not a profitable choice of detoxification of IFP. For instance, the TAC
357 using vacuum fermentations is 1.3- fold higher than that of SSF-E feeding a concentration
358 of 9 g/l of IFP [8] and substrate cost two times lower. Given that the final purification of IFP
359 and BA was not studied in this work, the profitability of SSF-E at concentrations of IFP
360 between 13.5 and 30 g/l will depend on the TAC of the final purification of IFP and BA.
361 However, the maximum purification cost of IFP and BA necessary in SSF-E to equal the
362 performance of 0 g/l of IFP was 47.3% and 8.6% of the current selling price of FuOL and
363 VaN, respectively.

364 Adsorption as well as liquid-liquid extraction can be used to recover simultaneously
365 IFP and butanol. Hence, although in this work we focus our attention in liquid-liquid
366 extraction, simultaneous detoxification and ABE production by adsorption needs to be
367 studied in future work. The selection between adsorption and liquid-liquid extraction will
368 depend on the regeneration system used and the qualities of the entrainer, such as
369 distribution coefficient, heat capacity, cost and selectivity, i.a. [10,44,45]. In addition, other
370 technical problems must be considered. For instance, emulsifiers may be required in liquid-

371 liquid extraction, or adsorption may need additional pretreatment units to minimize the
372 fouling [46].

373 **4. Conclusions**

374 The heat-integrated distillation system proposed in this work for the production of
375 ABE, BA and IFP allowed an energy saving around 73%. BA was an important value added in
376 ABE production by SSF-E. The SSF-E was an economical way to reduce the toxicity of IFP at
377 concentrations lower than 13.5 g/l. The substrate cost was the most important factor in the
378 economic evaluation when the concentrations of IFP were lower than 18 g/l. However,
379 when the concentrations of IFP were higher than 18 g/l the cost of recovery and purification
380 was the most important factor. Although the IFP and BA sale can become feasible SSF-E at
381 concentrations of IFP between 13.5 and 30 g/l, the energy requirements were between 1.2-
382 and 2.4-fold higher than that for SSF-E and IFP concentrations of 9 g/l, respectively. Instead
383 of the positive economic indicators of SSF-E, experimental and process simulations studying
384 the effects of mass transfer in the economy and controllability of the reactor and
385 purification system must be performed in future work. The toxicity of IFP must be reduced
386 in microorganisms that produce butanol to decrease the energy requirements of the
387 process. Given that ABE fermentation in the industry is usually performed using series-in-
388 tank systems, ISRR in series must be studied in future work.

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393

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571 Caption of figures

572 **Fig. 1.** *In situ* recovery reactor by liquid-liquid extraction and extractant regeneration

573 system. C2 is the column used to recovery ABE from the aqueous phase of the

574 reactor and decanters

575 **Fig. 2.** Strategy of simulation studied in this work for the economic optimization of a

576 simultaneous detoxification and reaction system

577 **Fig. 3.** Distillation system with partial recovery of oleyl alcohol (OAL) in the regeneration

578 column and with heat integration. OAL top at the top was 1000 kg/h. Q is heat,

579 VaN is Vanillin, BA is butyric acid, FuO is furfuryl alcohol, A is acetone, B is butanol

580 and E is ethanol. D is decanter.

581 **Fig. 4.** Performance indicators of *in situ* recovery production of ABE, furfuryl alcohol,

582 butyric acid and vanillin. The costs were estimated without including the final

583 separation system. The selling prices of butyric acid, furfuryl alcohol and vanillin

584 were nil. IFP: inhibitors from pretreatment; EP: economic potential.

585 **Fig. 5.** The economic potential of the reaction system and recovery units. The economic

586 potential was estimated at several concentrations and selling prices of inhibitors

587 from pretreatment (IFP) (a) Selling price of butyric acid of 2 \$/kg (b) Selling price of

588 butyric acid of 1 \$/kg, (c) Selling price of butyric acid of 0 \$

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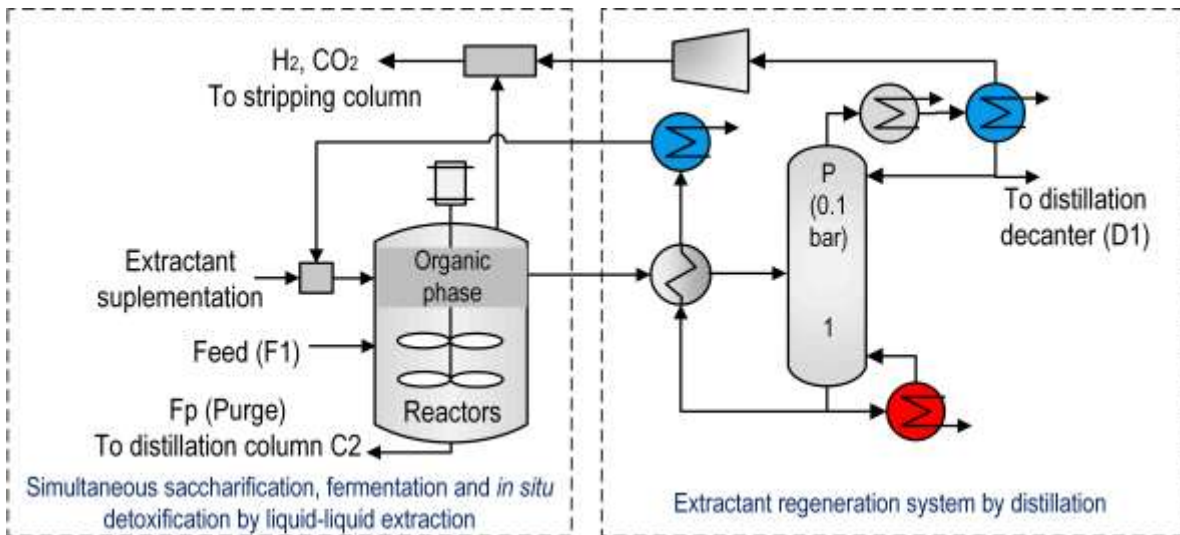
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593 Fig. 1.

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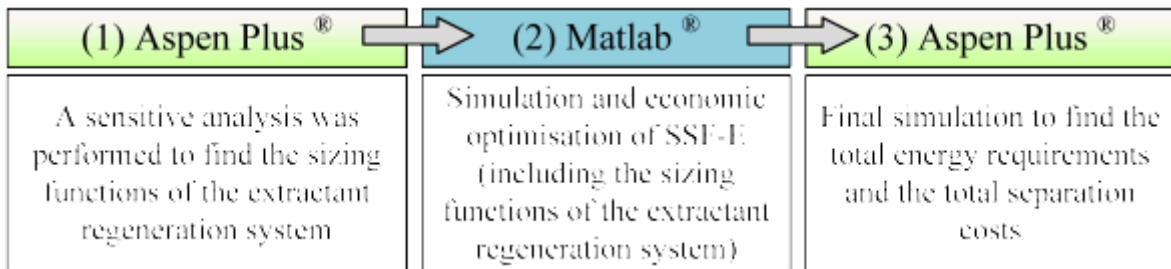
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609 Fig. 2



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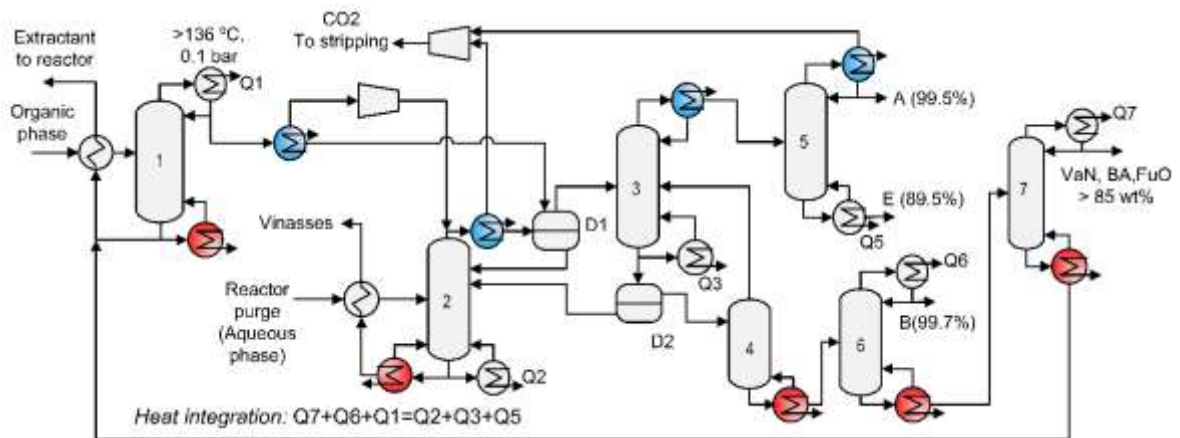
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628 Fig. 3.



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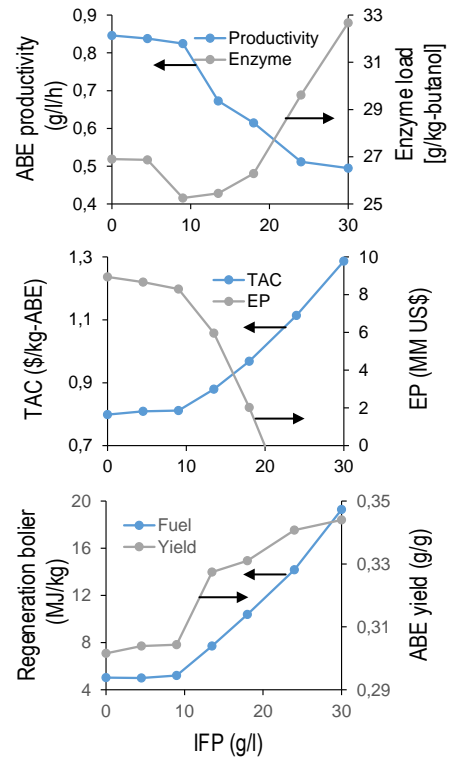
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645 Fig. 4



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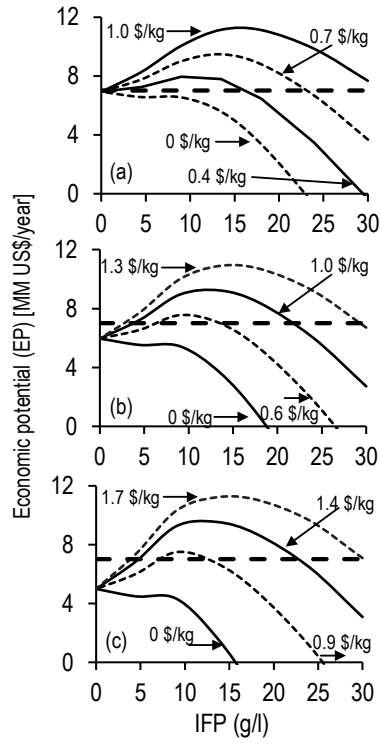
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Table 1

Partition coefficient of several solvents in oleyl alcohol (*350 °C)

Solvent	Partition coefficient	
	Experimental	UNIQUAC (30 °C)
Butanol (*119 °C)	3.7-3.8 [41]	3.9
Acetone (58 °C)	0.34-0.44 [41]	0.48
Ethanol (* 79 °C)	0.2-0.3 [24,41]	0.29
Acetic acid (*118 °C)	0.15-0.35 [24,41]	0.05
Butyric acid (*163 °C)	3.7 [41]	2.2
Furfural (*162 °C)	1.49-1.5 [24] ^b	1.2
Vanillin (*285 °C)	5.6-7.1 [24] ^b	11.8
HMF (*291 °C)	0.24-0.26 [24] ^b	0.05
2,5-DMF (*275 °C)	-	0.51
Furfuryl alcohol (*170°C)	-	2.6
Coumaric acid (*316°C)	-	10.6
Ferulic acid (*405°C)	-	4.4

*Boiling point

^b Extraction Temperature 34 °C

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Table 2
Economic and energy evaluation of SSF-E and end recovery system

IFP ^a (g/l)	IFP ^b (g/l)	B ^c (g/l)	Total annualized cost (\$/kg-ABE ^a)						Total energy requirement [MJ-fuel/kg- ABE ^a]
			Enzyme (4.3 \$/kg- enzyme)	Substrate (0.12 \$/kg- substrate)	Reactor investment	Recovery system		Total	
						<i>In situ</i> recovery unit	Total recovery and purification		
0	0	5.2	0.090	0.404	0.128	0.115	0.19	0.81	10.7
9	1.4	4.9	0.089	0.397	0.131	0.128	0.21	0.82	11.4
18	1.8	2.7	0.089	0.368	0.185	0.263	0.34	0.99	17.3
30	2.3	1.7	0.108	0.354	0.238	0.522	0.61	1.31	30.4

IFP (acetate concentration plus furan and phenolic concentrations)

^a The ABE flow was the flow of purified ABE

^b IFP titer in the reactor at the end of fermentation

^c Butanol titer in the reactor at the end of fermentation

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Table 3
Energy performance of distillation process for extractive system

Item	SSF-E (IFP of 0 g/l)		SSF-E ^b (IFP of 9 g/l)	
	Heat or Work (MJ/kg ABE)	Net (MJ fuel/kg ABE)	Heat or work (MJ/kg-ABE)	Net (MJ fuel/kg ABE)
Preheating 1 (extractant)	24.3	-	26.3	-
Preheating 2 (vinasses)	2.41	-	2.7	-
Compressor	0.06	0.18 ^c	0.06	0.19 ^c
Boiler				
1	4.62	5.77 ^a	5.18	6.48 ^a
2	3.86	2.98 ^b	3.94	2.39 ^b
3	0.98	0	1.09	0
4	0.78	0.86 ^b	0.92	1.02 ^b
5	0.39	0	0.38	0
6	0.7	0.82 ^a	0.86	1.02 ^a
7	0.04	0.06 ^a	0.24	0.3 ^a
Total	38.1	10.7	41.7	11.4
	ABE	VaN	ABE	VaN
Product flow (kg/h)	5184	-	5070	247
	BA	AB	BA	FuOL
	109	-	138	181

^{a,b,c} Fuel requirements assuming an energy efficiency of ^a0.8, ^b0.9 and ^c0.33

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