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Advanced purification of isopropanol and acetone from syngas fermentation

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Abstract

BACKGROUND: Isopropanol and acetone production by syngas fermentation is a promising alternative to conventional fossil carbon-dependent production. However, this alternative technology has not yet been scaled up to an industrial level owing to the relatively low product concentrations (about 5 wt% in total). This original research aims to develop cost-effective and energy-efficient processes for the recovery of isopropanol and acetone from highly dilute fermentation broth (>94 wt% water) for large-scale production (about 100 $\mathrm{kt_{IPA+AC}\ y^{-1}}$).

RESULTS: Vacuum distillation and pass-through distillation enhanced with heat pumps or multi-effect distillation were efficiently coupled with regular atmospheric distillation and extractive distillation in several innovative intensified downstream processes. Over 99.2% of isopropanol and 100% of acetone were recovered as high-purity end-products (>99.8 wt%). Advanced heat pumping (mechanical vapor recompression) and heat integration techniques were implemented to decrease total annual costs (0.109–0.137 USD $\mathrm{kg_{IPA+AC}}^{-1}$), reduce energy requirements (1.348–2.043 $\mathrm{kW_{th}}$ h $\mathrm{kg_{IPA+AC}}^{-1}$) and lower $\mathrm{CO_2}$ emissions (0.067–0.191 $\mathrm{kg_{CO2}\ kg_{IPA+AC}}^{-1}$), resulting in highly competitive recovery processes.

CONCLUSION: The proposed three novel isopropanol and acetone recovery processes from dilute broth significantly contribute to the expansion of sustainable industrial fermentation. Furthermore, this original research is the first one to develop novel pass-through distillation technology for the complex isopropanol–acetone–water system. All the designed processes are highly economically competitive and environmentally viable. In addition to recovering efficiently both isopropanol and acetone, the designed downstream processes offer the possibility to enhance the fermentation process by recycling all the present microorganisms and reducing fresh-water requirements.

Supporting information may be found in the online version of this article.

Keywords: isopropanol and acetone; syngas fermentation; downstream processing; pass-through distillation; process integration

INTRODUCTION

Increasing environmental concerns inevitably highlight the need for more sustainable manufacturing of commodity chemicals and materials.[1] Isopropanol and acetone are examples of essential platform chemicals that are mainly produced from fossil carbon sources. The total global market for these chemicals is about 10 billion USD,[2] with an expanding trend.[3] Isopropanol is an important industrial solvent and precursor, pharmaceutical ingredient, disinfectant, and fuel additive. Similarly, acetone has applications as an industrial solvent and platform chemical but can also be used for enhancing fuel performance.[2-4] In industry, isopropanol is primarily produced from propylene through direct or indirect hydration, while acetone is mainly produced as by-product of phenol in the cumene process. Even though these processes usually result in high conversion rates and selectivity, increasing feedstock costs and stricter environmental regulations are becoming limiting factors.[3] However, the manufacturing of these chemicals through fermentation processes is a promising sustainable alternative.[5,6]

To date, numerous research studies have explored the pathways for synthesizing acetone and isopropanol.[2-4,7-10] The main obstacle for commercialization is the low yield of carbohydrates that has been achieved so far.[2] However, LanzaTech has recently engineered *Clostridium autoethanogenum* and *C. autoethanogenum* strains to produce isopropanol and acetone from waste gases (industrial off-gases or syngas produced from biomass). This technology has already been tested at pilot scale,[2] but industrial scale has not been reached yet.[11] Due to product inhibition, concentrations of isopropanol and acetone in fermentation broth will certainly be below 10 wt%.[12] These low titters lead to a challenge for designing downstream processes, which is expected to be a significant cost contributor in large-scale processes.[1] However, few studies have been

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published on recovery of isopropanol and acetone from syngas fermentation broth,[13-15] mainly focusing on recovering only one of these components, and usually not on an industrial scale. Therefore, this original study focuses on conceptually designing eco-efficient large-scale recovery methods for both isopropanol and acetone.

Substrate gases for fermentation can be either waste gases from heavy industries or syngas formed by biomass gasification. These gases can be converted to mixtures of isopropanol and acetone by engineered bacteria.[11] As suggested earlier,[16,17] bacteria may be recycled to the fermentation if the initial recovery step ensures viability of the bacteria.

This original research is the first one to develop large-scale processes (production capacity 100 $\mathrm{kt_{IPA+AC}\ y^{-1}}$) for recovery of isopropanol and acetone from highly dilute fermentation broth (>94 wt% water). To ensure microbial viability, two options were proposed for the initial step in the recovery process: vacuum distillation and novel pass-through distillation. Accordingly, additional novelty in this research is pass-through distillation design for the complex isobutanol–acetone–water system and development of the required thermodynamic property model. Furthermore, several distillation steps were used to recover high-purity (about 99.8 wt%) final products with recoveries higher than 99%. Advanced heat pumping and heat integration techniques were applied to considerably reduce energy requirements and greenhouse gas emissions. For the evaluation of the designed processes, the economic (capital, operating and total recovery costs) and environmental impact (energy intensity, water consumption, CO_2 emissions, etc.) were calculated to determine the overall cost and energy efficiency. Besides effectively recovering fermentation products, proposed processes offer the possibility to recycle all present microorganisms and water to the fermentation process. Consequently, avoided loss of biomass and reduced need for fresh water may significantly enhance the fermentation. Thus, developed advanced downstream processes present substantial contribution to expansion of sustainable industrial fermentation.

METHODS

Process design and simulation

Recovery of isopropanol and acetone was designed for a large-scale industrial plant with a total isopropanol and acetone productivity of about 100 kt $\mathrm{y^{-1}}$. The feed stream for this process is broth taken from the fermenter. Since it had already been proven that the microorganisms can tolerate about 50 g $\mathrm{L^{-1}}$ of isopropanol and acetone,[18] and the mass ratio between produced isopropanol and acetone is 4:1,[2] it was considered that isopropanol and acetone concentrations should be 4 and 1 wt%, respectively. The concentration of acetate was determined relative to the concentration of isopropanol.[10] Additionally, some microorganisms and non-volatile inert components are present in the fermentation broth. These heavy components can be practically neglected in the simulations as they are removed in the first step, without evaporation. Nonetheless, fermentation broth is very dilute, containing over 94 wt% water, which is the main challenge for product purification. This stream (stream 1 in Tables 2-4) is at atmospheric pressure (1 bar), with a fermentation temperature of 30 °C.[8,9] Besides the highly dilute stream and the presence of living microorganisms, purification of syngas fermentation products is challenging due to the closeness of boiling points and the water–isopropanol azeotrope (Table 1).

The recovery process was designed in a way to initially separate isopropanol and acetone from the microorganisms and most of the water. Therefore, operating conditions for the first separation step were chosen to ensure viability of present microorganisms. Two different options were considered for this step: vacuum distillation and pass-through distillation. Microorganisms with most of the water may be recycled to the fermentation to avoid loss of biomass, reduce the need for fresh water and allow the upstream fermentation to operate in a closed loop.[16] Traces of acetate and minerals will also be recycled, but can be used by the microorganisms.[2] Furthermore, several distillation steps are needed to obtain high-purity final isopropanol and acetone products from the separated aqueous solution. Rigorous simulations for every step in the recovery process were developed in Aspen Plus.

When designing the isopropanol and acetone recovery process, all process decisions were focused on minimizing total energy requirements. Even though there is no theoretical guarantee of global optimum for non-convex mixed-integer nonlinear problems (MINLP) – such as the optimization of chemical processes – the minimization of external energy requirements reduces the total recovery costs. This is because OPEX dominates over CAPEX (except when considering extremely short payback periods), while a large part of OPEX is related to the cost of energy supply (both thermal and electrical energy usage). Some of the considered decision variables, which are discussed in more detail in the following sections, are: total number of trays in the columns, location of the feed tray, reflux ratio, distillate to feed ratio, vapor fraction, compression ratio, and so forth. Simultaneously, the constraints for effective process design are: temperature limitation in the initial separation step (due to presence of microorganisms), high recoveries of both acetone and isopropanol products, high purities of acetone and isopropanol products, high purity of the water stream that enables recycling to the fermentation, full recovery of LiBr brine and ethylene glycol solvent that ensures reusage, and so forth.

Economic analysis

To prove the economic competitiveness of the proposed recovery processes, a complete economic evaluation was conducted using a published NREL methodology[19] that accounts for both total capital (CAPEX) and operating (OPEX) costs. Calculation of the total CAPEX includes direct capital costs, related to the equipment purchase and installation, and indirect capital costs associated with costs for home office and construction, field expenses, prorateable expenses, project contingency, working capital, site development, additional piping, warehouse and solvent initial costs.[19] Installation costs for all process equipment units were estimated using published cost correlations,[20,21] whereby the Marshall and Swift cost index value used is 1638.2 (end of 2018). The total OPEX takes into account variable operating costs, related to the costs for utilities and make-up solvent, and fixed operating costs, determined by cost for labor, maintenance and property insurance.[19] The total annual costs (TAC) that account for both CAPEX and OPEX, and the minimum added prices (MASP) for isopropanol and acetone purification, were determined following the same methodology[19] using a 10-year payback period. Additionally, the effect of the assumed payback period on TAC was analyzed for all designed process configurations and is presented in Supporting Information, Data S1.

Sustainability metrics

The environmental impact of designed recovery processes was estimated by calculating the following sustainability metrics (lower values meaning better sustainability): energy intensity, water consumption, material intensity, greenhouse gas emissions, pollutants and toxic materials.[22]

Table 1. Boiling points (T_b) of pure components and azeotrope formation at 1 bar

Pure components		Azeotrope			
Component	T_b (°C)	Component	Mass fraction	T (°C)	Type
Acetone	56.25	Isopropanol	0.8717	80.23	Homogeneous
Isopropanol	82.25	Water	0.1283		
Water	100.00				
Acetic acid	117.95				

Table 2. Conditions and composition of the main process streams, process configuration vacuum distillation (VD)

Stream	1	2	3	4	5	6	7	8	9	10	11
Temperature (°C)	30.0	30.0	82.7	30.0	88.7	79.8	105.6	75.0	30.0	148.9	30.0
Pressure (bar)	1.000	0.043	1.300	1.000	1.312	1.300	1.232	1.200	1.000	1.504	1.000
Flowrate (kg h^{-1})	250 000	215 250	34 750	2511	32 239	11 638	20 601	12 802	10 038	14 402	1596
Mass fractions											
Water	0.9481	0.9980	0.6392	0.0014	0.6888	0.1386	0.9997	0.0000	0.0014	0.1110	1.0000
Isopropanol	0.0401	0.0000	0.2885	0.0005	0.3109	0.8613	0.0000	0.0000	0.9985	0.0000	0.0000
Acetone	0.0100	0.0000	0.0721	0.9981	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Acetic acid	0.0018	0.0020	0.0002	0.0000	0.0002	0.0000	0.0003	0.0000	0.0000	0.0000	0.0000
Ethylene glycol	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.8890	0.0000

Table 3. Conditions and composition of the main process streams, process configuration PTD-VRC

Stream	1	2	3	4	5	6	7	8
Temperature (°C)	30.0	26.3	26.3	27.0	30.2	30.2	33.3	81.8
Pressure (bar)	1.000	0.043	0.043	0.042	0.043	0.043	0.041	1.200
Flowrate (kg h^{-1})	250 000	2299	247 701	32 423	241 942	215 278	85 656	34 722
Mass fractions								
Water	0.9481	0.5260	0.9520	0.6482	0.9974	0.9978	0.5229	0.6401
Isopropanol	0.0401	0.2662	0.0380	0.2885	0.0007	0.0003	0.1232	0.2870
Acetone	0.0100	0.2072	0.0083	0.0626	0.0000	0.0000	0.0293	0.0722
Acetic acid	0.0018	0.0006	0.0018	0.0007	0.0019	0.0019	0.0003	0.0007
LiBr	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.3243	0.0000
Ethylene glycol	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

Stream	9	10	11	12	13	14	15	16
Temperature (°C)	55	30.0	88.9	79.9	75	30.0	149.8	30.0
Pressure (bar)	0.043	1.000	1.312	1.300	1.200	1.000	1.504	1.000
Flowrate (kg h^{-1})	50 934	2511	32 211	11 574	12 802	9983	14 392	22 228
Mass fractions								
Water	0.4431	0.0013	0.6899	0.1391	0.0000	0.0020	0.1105	0.9989
Isopropanol	0.0115	0.0007	0.3093	0.8609	0.0000	0.9980	0.0000	0.0000
Acetone	0.0000	0.9980	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Acetic acid	0.0000	0.0000	0.0008	0.0000	0.0000	0.0000	0.0000	0.0011
LiBr	0.5454	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Ethylene glycol	0.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.8895	0.0000

Abbreviations: PTD-VRC, pass-through distillation coupled with vapor recompression; LiBr, lithium bromide.

- Energy intensity is a measure of heat and electrical energy requirements expressed per kilogram of product.[22] Total energy requirements take into account both thermal and electrical energy, using the electrical-to-thermal conversion factor. A conservative value of 2.5, which accounts for the overall energy efficiency, was assumed.[23]
- Water consumption is the amount of fresh water used per kilogram of product.[22] This metrics accounts for cooling water, with loss assumption of 7%,[22] and additional water that includes all inefficiencies in steam generation and usage, with the assumption that 70% of steam condensate is recovered.[24]

Table 4. Conditions and compositions of the main process streams, process configuration PTD-MED

Stream	1	2	3	4	5	6	7	8
Temperature (°C)	30.0	26.3	26.3	27.0	30.2	30.2	32.3	81.8
Pressure (bar)	1.000	0.043	0.043	0.042	0.043	0.043	0.041	1.200
Flowrate (kg h^{-1})	250 000	2299	247 701	32 423	241 942	215 278	90 417	34 710
				Mass fractions				
Water	0.9481	0.5260	0.9520	0.6482	0.9974	0.9978	0.4729	0.6405
Isopropanol	0.0401	0.2662	0.0380	0.2885	0.0007	0.0003	0.1919	0.2866
Acetone	0.0100	0.2072	0.0083	0.0626	0.0000	0.0000	0.0277	0.0722
Acetic acid	0.0018	0.0006	0.0018	0.0007	0.0019	0.0019	0.0003	0.0007
LiBr	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.3072	0.0000
Ethylene glycol	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

Stream	9	10	11	12	13	14	15	16
Temperature (°C)	55.0	30.0	88.9	79.9	75.0	30.0	149.7	30.0
Pressure (bar)	0.043	1.000	1.312	1.300	1.200	1.000	1.504	1.000
Flowrate (kg h^{-1})	55 695	2510	32 320	11 569	12 802	9966	14 406	22 230
				Mass fractions				
Water	0.3686	0.0012	0.6903	0.1403	0.0000	0.0020	0.1113	0.9989
Isopropanol	0.1326	0.0006	0.3089	0.8596	0.0000	0.9980	0.0000	0.0000
Acetone	0.0000	0.9982	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Acetic acid	0.0000	0.0000	0.0008	0.0000	0.0000	0.0000	0.0000	0.0011
LiBr	0.4987	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Ethylene glycol	0.0000	0.0000	0.0000	0.0000	1.0000	0.0000	0.8887	0.0000

Abbreviations: PTD-MED, pass-through distillation coupled with multi-effect distillation; LiBr, lithium bromide.

- Material intensity represents the amount of formed waste[22] or non-product[25] per kilogram of product.
- Greenhouse gas emission accounts for the amount of carbon dioxide (CO_2) emitted per kilogram of product.[22] Published methodologies were used for determining these emissions,[21,26] whereby CO_2 emissions are directly related to energy use. Differentiation was made between green electricity (electricity obtained from renewable sources) and grey electricity (electricity obtained from fossil fuels). If green electricity is available, CO_2 emissions are related only to thermal energy usage. Contrarily, if grey electricity must be used, CO_2 emissions are associated with both thermal and electrical energy usage.
- Pollutants and toxic materials metrics present the amount of emitted pollutants and toxic materials formed per kilogram of product.[22]

RESULTS AND DISCUSSION

This section presents the results of the process design for recovery of isopropanol and acetone from the fermentation broth. Additionally, outcomes of the techno-economic evaluation and calculation of sustainability metrics are provided and analyzed.

Separating products from the fermentation broth

The first step in the recovery process is separation of isopropanol and acetone from the remaining fermentation broth, whereby temperature conditions are kept appropriate for the microorganisms. Vacuum distillation and pass-through distillation were designed for this initial separation.

Vacuum distillation

To ensure that the operating temperature does not exceed the fermentation temperature (30 °C), isopropanol and acetone can be separated from most of the fermentation broth using vacuum distillation. This process configuration is referred to as VD (see Fig. 1), which is further discussed below. Thermodynamic properties were specified with the NRTL property method coupled with the Hayden O'Connell model for vapor phase association[27] due to the presence of acetic acid. Vacuum distillation is performed in distillation column C1, which was designed assuming structured packing type Sulzer Mellapak 250 for its internals.[28] A condenser pressure of 0.032 bar was selected, with a pressure drop of 0.225 mbar per theoretical stage.[28] At this operating pressure, the temperature in this column drops from about 30 °C at the bottom to only 10 °C at the top. Consequently, cooling water cannot be used for the cooling and more expensive chilled water is required. Additionally, the heating duty required for this column is very high (about 22 MW) due to the large feed flowrate. However, the relative closeness of top and bottom temperatures offers the possibility to apply mechanical vapor recompression (MVR) to this column.[29] This heat pump design implies compressing vapor coming from the top of a distillation column and using the compressed vapor to evaporate liquid from the bottom of the column.[30] The coefficient of performance (COP) of this system is the ratio of exchanged heating duty (between compressed top vapor and bottom liquid) and required compressor duty. The COP of MVR for column C1 (8.8) is significantly higher than the electrical-to-thermal-energy conversion factor, for which 2.5 is a conservative value.[23] Therefore, MVR drastically reduces energy requirements for this separation.

Isopropanol and acetone are completely separated from the remaining fermentation broth in this first distillation step. The top stream contains about 28.8 wt% isopropanol and 7.2 wt% acetone and requires further processing. The bottom stream contains most of the water, all microorganisms and all other inert compounds. As mentioned, this stream may be

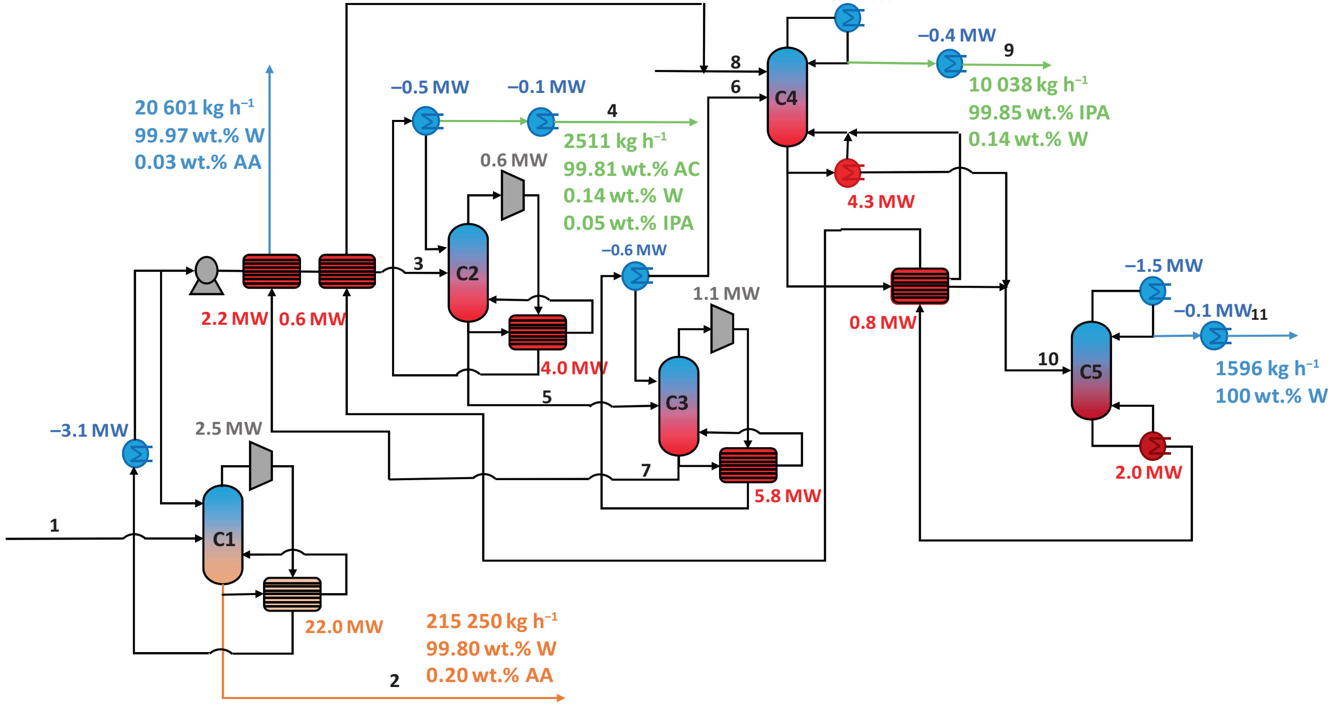

Figure 1. Flowsheet of isopropanol and acetone recovery process using vacuum distillation (VD) process configuration (W - water, IPA - isopropanol, AC - acetone, AA - acetic acid).

recycled to fermentation to enhance the performance of the upstream process.

Pass-through distillation

The described vacuum distillation results in a very low condensation temperature (10 °C). Consequently, usage of chilled water is required. Pass-through distillation (PTD) is a new separation technique that can avoid such a low condensation temperature. This can be of even greater significance if the upper temperature limit is lower than the assumed 30 °C since it would result in higher vacuum and, consequently, lower condensation temperature. The working principle of PTD is decoupling of evaporation and condensation by using an absorption–desorption loop with concentrated lithium bromide (LiBr) solution as absorbent fluid.[31,32] PTD consists of four steps: evaporation, absorption, desorption and condensation. First, part of the liquid feed stream is evaporated, and the formed vapor is absorbed using the absorbent fluid. These evaporation and absorption steps can be integrated into one process unit, called the stripping–absorption module (SAM), which does not require external heating.[33] After leaving the SAM unit, the absorbed components are evaporated from the diluted absorbent fluid and then condensed. As a result, evaporation can be performed at lower pressure (and temperature) that does not harm heat-sensitive compounds, while condensation can operate at higher pressure (and temperature), which allows usage of cheaper cooling utilities. Besides suitability to heat-sensitive materials and lower operating costs due to elimination of expensive refrigeration utilities, the benefit of PTD is reduced equipment size compared to vacuum distillation technologies, resulting in lower investment costs. Furthermore, energy requirements are highly competitive as compared to distillation.[32] More details about PTD and SAM are presented in Supporting Information, Data S1.

Designing a PTD recovery process is challenging due to the presence of an absorbent fluid. A reliable thermodynamic property model is needed. Therefore, interactions between the electrolyte absorbent (LiBr) and four polar solvents (water, isopropanol, acetone and acetic acid) were taken into account. The ElecNRTL-RK, electrolyte-NRTL model coupled with the Redlich–Kwong equation of state, was chosen,[34] since it describes complex systems using binary interactions. Experimental data[35-38] for binary systems were used to determine values of binary interaction parameters (BIPs). More information about developing the property model and the obtained values of BIPs are given in Supporting Information, Data S1.

As mentioned, the evaporation and absorption parts of PTD can be coupled in the SAM unit. To improve the performance of the PTD process by lowering potential product losses, and increasing isopropanol and acetone concentration in vapor that is being sent to the absorption part, SAM was preceded by stripping column C1 (see Figs 2 and 3, further discussed below). Isopropanol and acetone concentrations are maximized in the outlet vapor from this column, before these compounds are absorbed using concentrated LiBr solution. The liquid phase remaining from the evaporation step contains most of the water, microorganisms and inert compounds, and may be recycled to the fermentation. The selected operating pressure for the SAM unit (0.0432 bar) ensures complete evaporation while maintaining a temperature of 30 °C (Fig. 4). The vapor fraction in SAM (0.11) was selected such that the isopropanol recovery in the formed vapor was more than 99% (Fig. 4). Subsequent absorption of this vapor by LiBr solution releases heat that is transferred by heat pipes to the evaporation part of SAM.[33] The flowrate of absorbent fluid relative to the

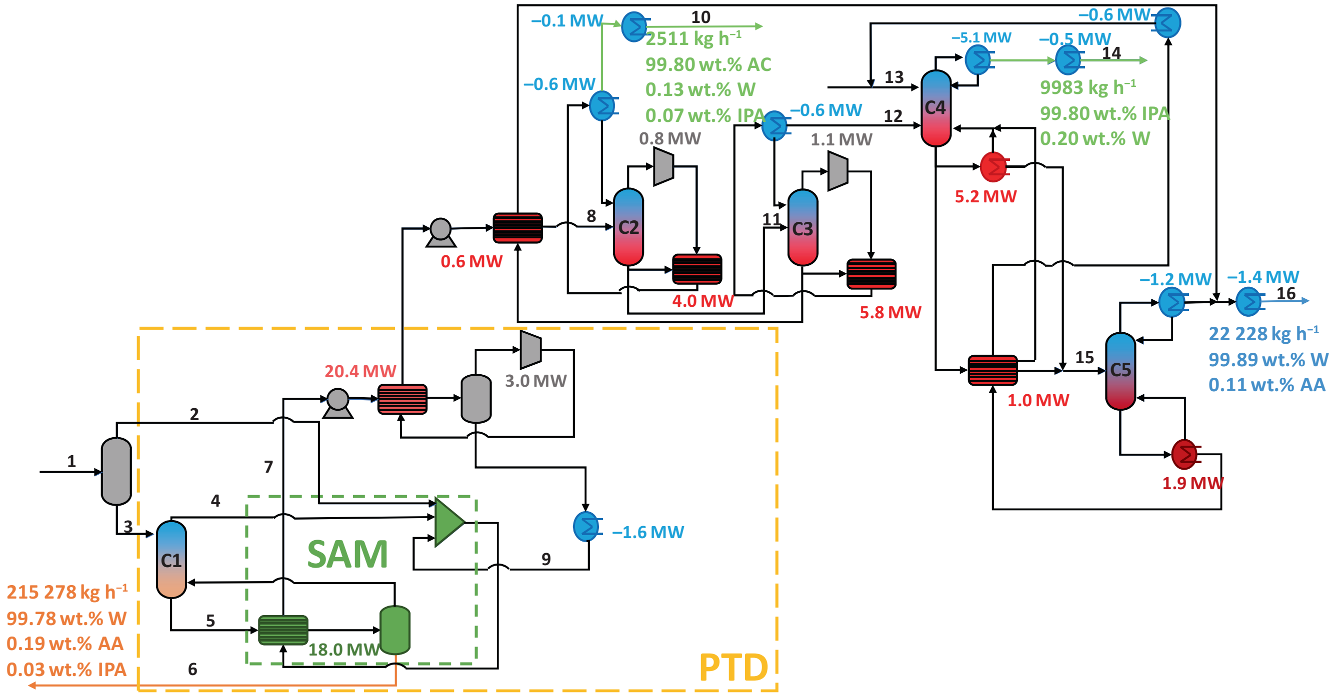

Figure 2. Flowsheet of isopropanol and acetone recovery process using pass-through distillation coupled with vapor recompression (PTD-VRC) process configuration (W - water, IPA - isopropanol, AC - acetone, AA - acetic acid).

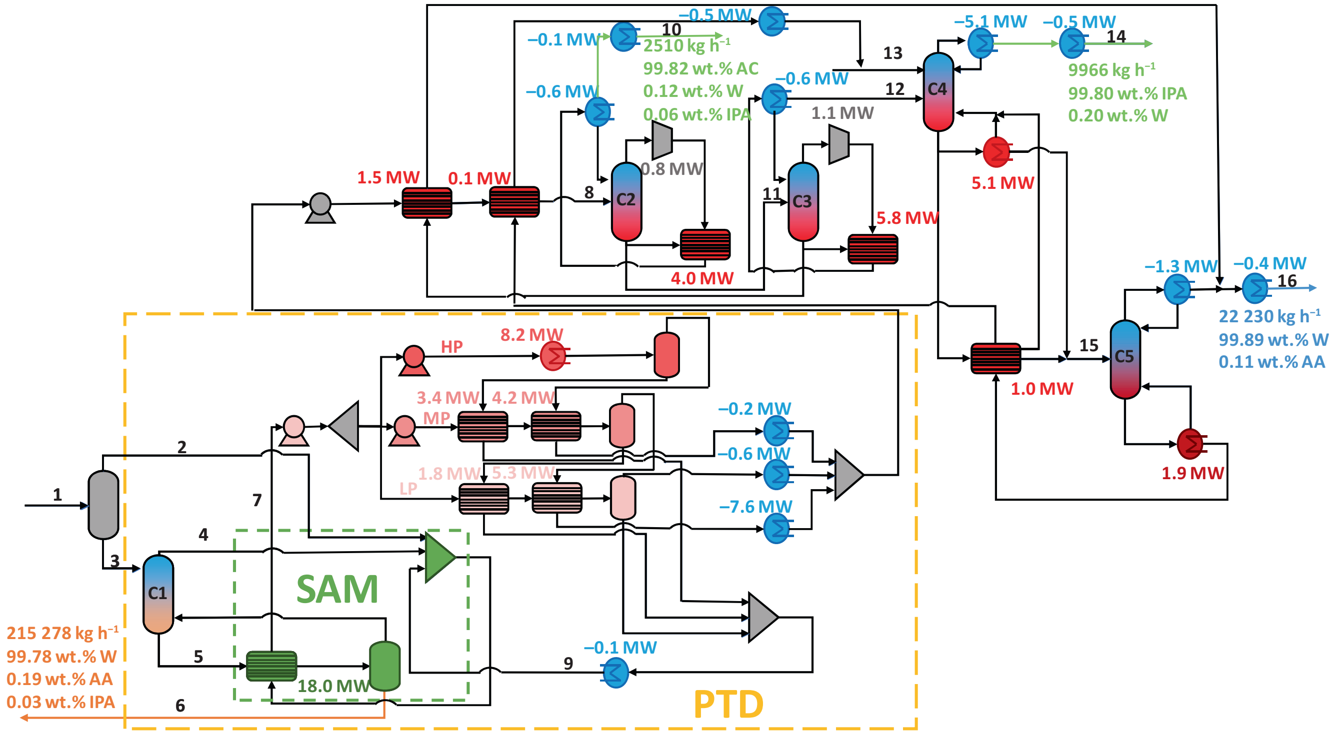

Figure 3. Flowsheet of isopropanol and acetone recovery process using pass-through distillation coupled with multi-effect distillation (PTD-MED) process configuration (W - water, IPA - isopropanol, AC - acetone, AA - acetic acid).

flowrate of vapor feed (1.6 on mass basis) was determined such that the diluted brine could provide heat for the evaporation step. Consequently, effective heat recovery from the absorption to evaporation part was achieved.

After SAM, the diluted brine is regenerated and recycled in a continuous circuit.[32] Previously absorbed isopropanol and acetone, with some water, are desorbed from the diluted stream and then condensed. Two alternative approaches were

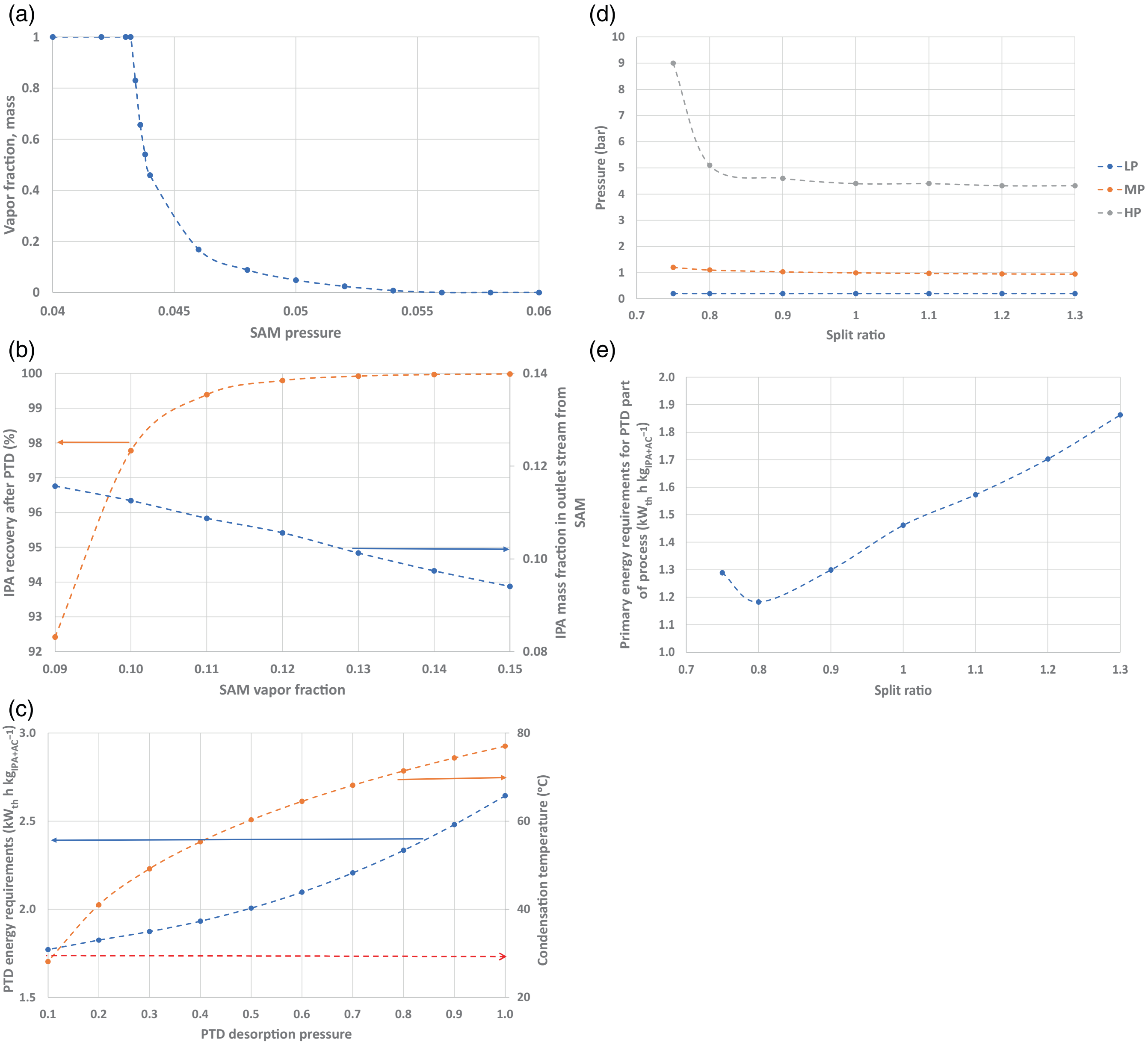

Figure 4. Operating parameters for pass-through distillation (PTD): (a) pressure in stripping–absorption module (SAM) unit; (b) defined vapor fraction in SAM unit; (c) desorption pressure in pass-through distillation coupled with vapor recompression (PTD-VRC) configuration; (d) split ratio in pass-through distillation coupled with multi-effect distillation (PTD-MED) configuration – high pressure (HP), medium pressure (MP) and low pressure (LP) pressure steam; (e) split ratio in PTD-MED configuration – energy requirements.

considered for desorption and condensation: heat-pump (vapor recompression) assisted desorption and multi-effect distillation. These process configurations are referred to as PTD-VRC and PTD-MED, respectively (Figs 2 and 3).

In PTD-VRC, the desorbed vapor is compressed to provide heat for desorption. This heat pump design was applied because evaporating isopropanol and acetone from diluted brine is very energy intensive. The operating pressure for this part of the PTD (0.2 bar) was chosen to minimize energy requirements for PTD while keeping the condensation temperature (about 41 °C) appropriate for using cheaper cooling water (Fig. 4). The coefficient of performance (COP) of this heat pump system is 6.75. Since this value is again much higher than the conservative value of electrical to thermal energy conversion factor of 2.5,[23] enhancing the desorption step with vapor recompression significantly improves energy efficiency. After the desorption step, recovered brine can be reused in the SAM unit.[32] The separated products mixture contains about 28.7 wt% isopropanol and 7.2 wt% acetone, whereby recovery from the fermentation broth is 99.4% and 100% for isopropanol and acetone, respectively.

In the alternative configuration (PTD-MED), concentrated brine is regenerated in three MED stages such that the feed stream is separated into high-pressure (HP), medium-pressure (MP) and low-pressure (LP) streams. The split ratio between these streams (the ratio between flowrates of HP and MP, as well as between MP and LP) determines the minimum pressure difference needed for heat exchange. The pressure of the LP stream (0.2 bar) was

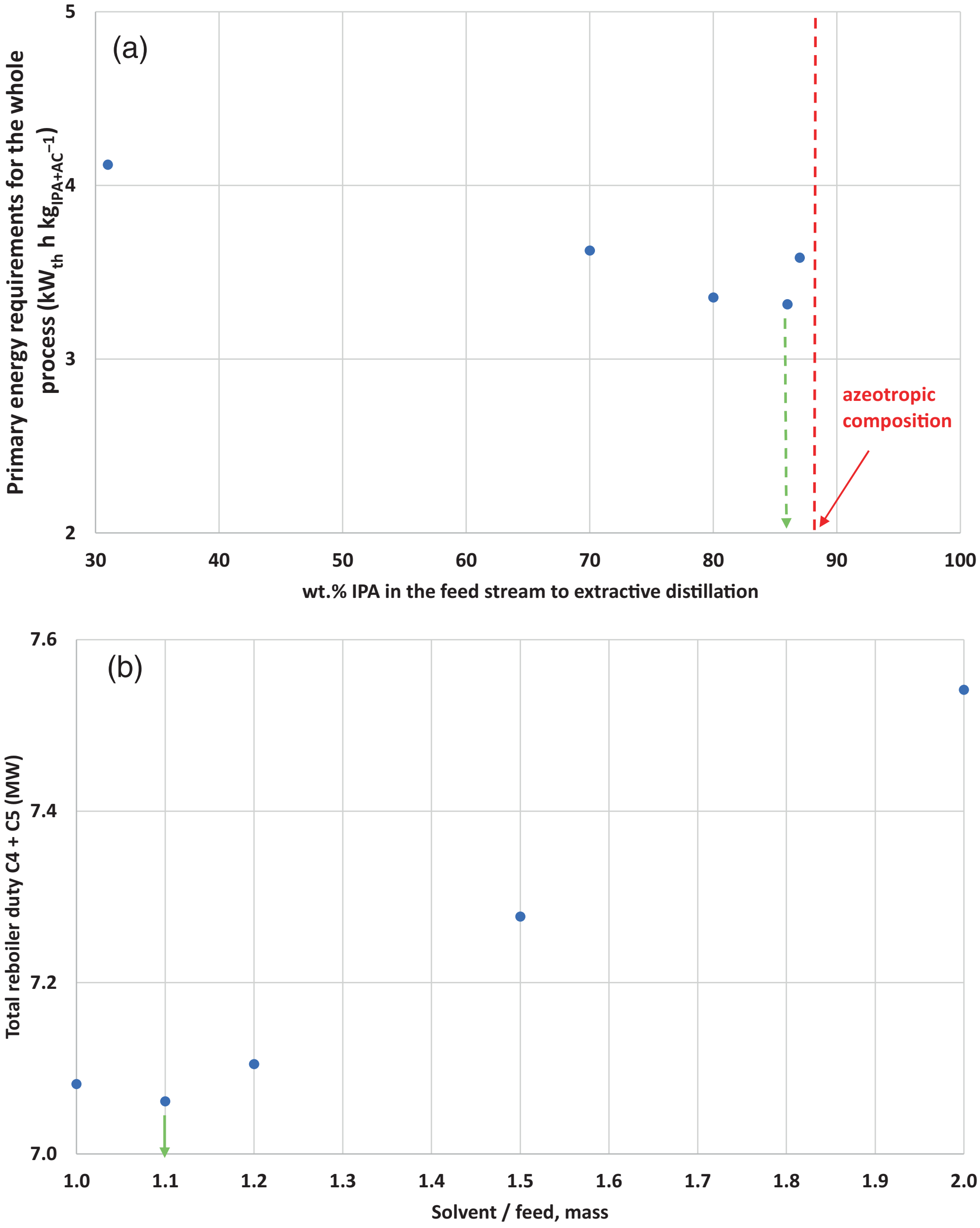

Figure 5. (a) Isopropanol concentration after preconcentration (energy requirements on *y*-axis are prior to implementing heat pumping and heat integration). (b) Solvent-to-feed ratio for extractive distillation.

determined such that its condensation is possible using cooling water rather than chilled water. With increasing split ratio, flowrates of higher pressure streams increase. Consequently, required pressures of HP and MP decrease, but more external heating is needed to heat the HP stream. To achieve the minimum energy requirements and reasonable pressures, a split ratio of 0.8 was chosen (Fig. 4). The operating pressures of HP and MP are 5.1 bar and 1.1 bar, respectively. Enhancing desorption with MED results in about 64% reduction in external heating requirements relative to simple desorption from the unseparated diluted brine (from about 23 MW to about 8 MW). The recovered brine can be recycled to the SAM unit.[32] The stream with separated products contains about 28.7 wt% isopropanol (99.2% recovery) and 7.2 wt% acetone (100% recovery).

Acetone purification

The separated isopropanol and acetone mixture from the fermentation broth, either by vacuum distillation (VD) or by PTD coupled with vapor recompression (PTD-VRC) or multi-effect distillation (PTD-MED), needs to be pumped to atmospheric pressure for purification. In the next distillation column C2, acetone, being the most volatile component (Table 1), is recovered (100% recovery) in the distillate at high purity (about 99.8 wt%), while a mixture of isopropanol and water is obtained as the bottom product.

As the feed stream to this column is subcooled liquid, it is preheated by implementing heat integration, which will be discussed in a later section. Even after heating the feed stream, required reboiler duty for acetone separation is about 4.0 MW. However, since this column is separating relatively close-boiling components, MVR can be applied to reduce energy requirements. COP for this MVR system is in the range of 5.2–6.5, depending on the design of the initial separation step (VD, PTD-VRC or PTD-MED). In all cases, applying heat pumping to this step results in significant energy savings.

Isopropanol purification

Separation of high-purity isopropanol from aqueous solution is challenging due to an azeotrope (Table 1). Following recommendations from the literature,[39-44] extractive distillation with ethylene glycol was chosen for final isopropanol dehydration. Nonetheless, since the bottom product from column C2 contains only about 31.1 wt% of isopropanol, preconcentration is needed prior to dehydration by extractive distillation. This is done in distillation column C3, where concentrated isopropanol solution is obtained as the top product, while pure water is obtained at the bottom. As the azeotropic composition is approached in the distillate, energy requirements for the preconcentration step increase, but subsequent dehydration becomes less energy intensive. Therefore, energy requirements for the overall process (without implementing any heat integration and heat pumping) were analyzed as function of the concentration of isopropanol after preconcentration (Fig. 5). The total energy requirements decrease up to about 86 wt% of isopropanol in the C3 distillate, so this extent of preconcentration is selected. The bottom stream of this column is pure water, which can be cooled and recycled to the fermentation to decrease the need for fresh water. Due to the closeness of boiling points of components that are being separated, the reboiler duty required for column C3 is relatively high (about 5.8 MW). Nevertheless, MVR can also be applied to this column, with a COP in the range of 5.2–5.4.

The preconcentrated isopropanol solution is further dehydrated using extractive distillation with ethylene glycol in column C4. The top stream from this column is high-purity (99.8 wt.%) isopropanol. The bottom stream contains ethylene glycol and remaining water, and is sent to solvent recovery column C5. The ethylene glycol is recovered as the bottom stream from column C5 for reuse in column C4. The remaining water is recovered at 100 wt % purity as the top product from column C5, and can be cooled and recycled to the upstream process. The ratio of ethylene glycol to feed flowrate (1.1, mass basis) was determined to minimize energy requirements for columns C4 and C5 (Fig. 5). Owing to large differences between top and bottom temperatures from columns C4 and C5, MVR is not suitable. However, since recovered solvent from column C5 needs to be cooled before reuse in column C4,[40] this stream can be used to evaporate part of the bottom liquid from column C4. This heat integration reduces the need for external heating for column C4 by about 16–17%.

Columns C2, C3, C4 and C5 operate at atmospheric pressure, with sieve trays and a pressure drop of 8 mbar per tray.[45] Details about these distillation columns are presented in Supporting Information, Data S1.

Full isopropanol and acetone recovery processes

The process flowsheets of the three designed process configurations – VD, PTD-VRC and PTD-MED – are presented in Figs 1–3, respectively. The conditions and compositions of the main process streams for these configurations are shown in Tables 2–4, respectively. All three process designs recover acetone and isopropanol each at 99.8 wt% purity, with recoveries of 100% and more than 99.2%, respectively. At the same time, process conditions were designed such that the viability of present microorganisms is not harmed. Even though additional experimental validation might be needed, it has been shown that microorganisms can survive exposing fermentation broth to vacuum.[46-48] If also applicable in the current case, the separated microorganisms in the aqueous stream can be recycled to the upstream process. Additionally, if some CO_2 is present in the fermentation broth, the proposed processes can be expanded by adding an initial degassing step under reduced pressure. In case some products are also removed, they should be captured with water in an additional stripping column and returned to the recovery process. Furthermore, a fermentation broth temperature higher than 30 °C will not greatly affect the design of the recovery process. For

Table 5. Comparison of economic indicators and sustainability metrics

	VD	PTD-VRC	PTD-MED
Economic indicators			
CAPEX (USD)	28 385K	28 422K	24 724K
OPEX (USD y^{-1})	8110K	8441K	11 199K
OPEX (USD kg_{IPA+AC}^{-1})	0.081	0.084	0.112
TAC (USD y^{-1})	10 949K	11 284K	13 671K
TAC (USD kg_{IPA+AC}^{-1})	0.109	0.113	0.137
MASP (USD kg_{IPA+AC}^{-1})	0.119	0.123	0.146
Sustainability metrics			
Thermal energy requirements (kW_{th} h kg_{IPA+AC}^{-1})	0.502	0.566	1.214
Electrical energy requirements (kW_e h kg_{IPA+AC}^{-1})	0.338	0.418	0.331
Primary energy requirements (kW_{th} h kg_{IPA+AC}^{-1})	1.348	1.612	2.043
CO_2 emission[a] (kg_{CO2} kg_{IPA+AC}^{-1})	0.221/0.067	0.264/0.073	0.342/0.191
Water consumption (m_w^3 kg_{IPA+AC}^{-1})	0.145	0.162	0.261
Water loss (m_w^3 kg_{IPA+AC}^{-1})	0.011	0.012	0.019
Pollutant emission ($kg_{pollutant}$ kg_{IPA+AC}^{-1})	0	0	0
Toxic materials emission ($kg_{toxic\ materials}$ kg_{IPA+AC}^{-1})	0	0	0

Abbreviations: VD, vacuum distillation; PTD, pass-through distillation; PTD-VRC, PTD coupled with vapor recompression; PTD-MED, PTD coupled with multi-effect distillation; CAPEX, capital expenditures; OPEX, operating expenditures; TAC, total annual costs; MASP, minimum added selling prices.
[a] Grey/green electricity.

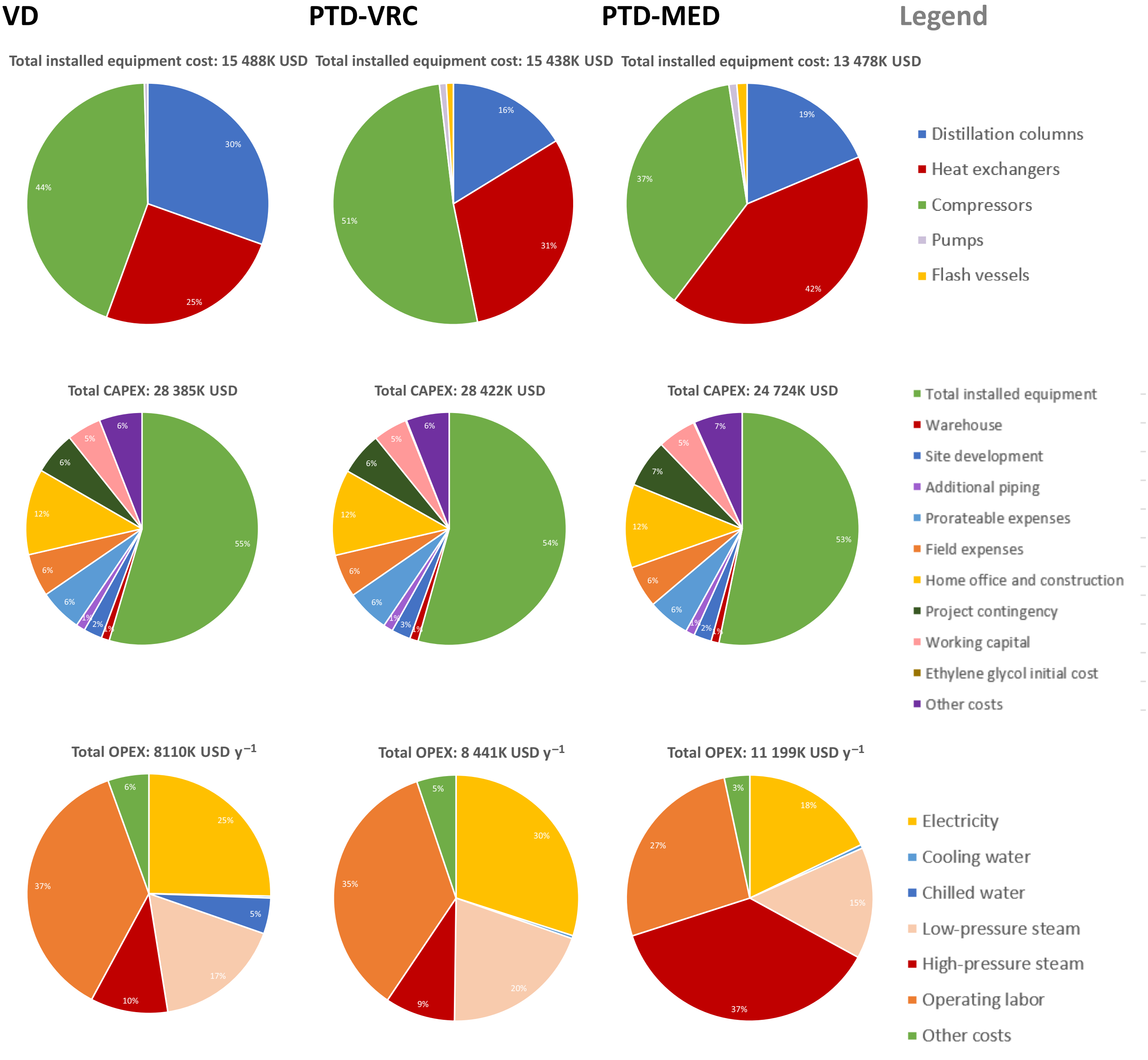

Figure 6. Comparison of economic indicators for all processes.

example, with a fermentation broth temperature of 37 °C in VD process configuration, the required pressure in column C1 would increase to 0.052 bar, while total heating requirements for distillation columns would alter for less than 0.5%. Therefore, the proposed processes are suitable for recovery of isopropanol and acetone from fermentation broths of different temperatures.

Besides MVR, additional heat integration is proposed to further reduce energy requirements. As previously mentioned, the water–isopropanol–acetone mixture separated from the rest of the fermentation broth, either by VD, PTD-VRC or PTD-MED, becomes subcooled liquid after pumping to atmospheric pressure. Therefore, preheating this stream to its boiling point can reduce the reboiler duty for column C2 and, consequently, the compressor duty required in the MVR system applied to this column. In all process configurations, pure water from the bottom of the isopropanol preconcentration column C3 was used to preheat the feed stream to the acetone purification column C2. The heat capacity of this water stream in PTD-VRC is sufficient to preheat the water–isopropanol–acetone mixture. However, in VD and PTD-MED, additional heating is needed to preheat this stream to its boiling point. As ethylene glycol needs to be further cooled after evaporating part of the bottom liquid from column C4,[40] this stream can be used to preheat the feed stream to column C2. In this way, sufficient heat is provided in both VD and PTD-MED. These heat integrations reduced the reboiler duty for column C2 by about 41% (from 6.8 to 4.0 MW), about 12% (from 4.6 to 4.0 MW) and about 28% (from 5.6 to 4.0 MW) in VD, PTD-VRC and PTD-MED, respectively.

The proposed heat pumping and heat integration significantly reduce the overall energy requirements by using heat content of hot process streams to heat cold process streams. Detail pinch analysis before and after enhancing the processes are provided in Supporting Information, Data S1. As a result of heat pumping, the overlapping areas of hot and cold composite curves are increased. Consequently, the energy amount that can be recovered in the processes is significantly enlarged, resulting in lower requirements for external heating and cooling.

Economic analysis

Economic comparison between all three designed process configurations is presented in Table 5 and Fig. 6. Total installation costs are 15 488K, 15 438K and 13 478K USD for VD, PTD-VRC and PTD-MED, respectively. The largest contribution to equipment cost is due to compressors in the case of VD (about 44%) and PTD-VRC (about 51%), due to heat pump systems, and heat exchangers used in multi-effect distillation for PTD-MED (about 42%).

CAPEX are 28 385K, 28 422K and 24 724K USD for VD, PTD-VRC and PTD-MED, respectively. For all process configurations, the main contribution to CAPEX is the installed equipment (about 53–55%). Therefore, recovering isopropanol and acetone using pass-through distillation coupled with multi-effect distillation (PTD-MED) is the best option in terms of capital investment, due to its the lower equipment cost.

OPEX for VD, PTD-VRC and PTD-MED are 8110K, 8441K and 11 199K USD y^{-1}, respectively, with utilities as the main cost contributor (about 57%, 60% and 70%, respectively). Among utilities, electricity costs dominate OPEX for VD and PTD-VRC (about 25% and 30%) due to implemented heat pump systems. For PTD-MED, high-pressure steam costs dominate (about 37%) due to evaporation of the HP stream and heating the solvent recovery column C5. Per kilogram of recovered isopropanol and acetone, OPEX costs are 0.081, 0.084 and 0.112 USD $kg_{IPA+AC}{}^{-1}$ for VD, PTD-VRC and PTD-MED, respectively. Therefore, VD and PTD-VRC designs are more appropriate than PTD-MED in terms of operating costs. However, cost for utilities highly depends on the site location, whereas the used costs are fixed according to literature recommendations.[20] If the unit cost ratio for heating to electricity is much lower than the value assumed, PTD-MED becomes the optimal process configuration. Alternatively, if using electricity is more favorable, then the VD and PTD-VRC designs are better options.

The total annual cost, taking into account both CAPEX and OPEX, is 10 949K, 11 284K and 13 671K USD y^{-1}, corresponding to 0.109, 0.113 and 0.137 USD $kg_{IPA+AC}{}^{-1}$, for VD, PTD-VRC and PTD-MED, respectively. Since market prices for isopropanol and acetone are assumed to be 1.09–1.32 and 0.88–1.05 USD kg^{-1}, respectively,[14,49] all proposed process designs are highly economically competitive. Furthermore, to expand the flexibility of the performed economic evaluation, the influence of payback period on total costs is analyzed and presented in Supporting Information, Data S1. The designed recovery processes are proven to be competitive even with shorter payback periods (e.g., for a payback period of 3 years, recovery costs for all three process designs are lower than 0.2 USD $kg_{IPA+AC}{}^{-1}$). Lastly, the added minimum selling price (MASP) for recovered products is 0.119, 0.123 and 0.146 USD $kg_{IPA+AC}{}^{-1}$ for VD, PTD-VRC and PTD-MED, respectively.

Sustainability metrics

Table 5 gives an overview of the environmental impact of the proposed processes.

- *Energy intensity*: Owing to the need for heating the HP stream in the multi-effect distillation, thermal energy requirements are the highest for PTD-MED (1.214 kW_{th} h $kg_{IPA+AC}{}^{-1}$). Conversely, electrical energy requirements are the highest for PTD-VRC (0.418 kW_e h $kg_{IPA+AC}{}^{-1}$), mainly due to the compressors used in heat-pump-assisted desorption in PTD and MVR systems. The primary energy requirements, which take into account both thermal and electrical energy, are 1.348, 1.612 and 2.043 kW_{th} h $kg_{IPA+AC}{}^{-1}$ for VD, PTD-VRC and PTD-MED, respectively. Lower concentrations of isopropanol and acetone in the feed stream would lead to more energy intensive recovery processes. Nonetheless, the proposed recovery processes are still highly competitive for treating more dilute fermentation broths (e.g. primary energy requirements for VD process configuration are lower than 2 or 3 kW_{th}h $kg_{IPA+AC}{}^{-1}$ for 2.5 or 1.2 wt% total isopropanol and acetone in the feed stream, respectively).
- *Water consumption*: PTD-MED requires most fresh water (0.261 m^3 $kg_{IPA+AC}{}^{-1}$), while PTD-VRC and VD need less (0.162 and 0.145 m^3 $kg_{IPA+AC}{}^{-1}$). This is mainly due to condensation of HP, MP and LP streams and higher external heating requirements. Water losses are also the highest for this configuration (0.019 m^3 $kg_{IPA+AC}{}^{-1}$).
- *Material intensity*: Besides high-purity isopropanol and acetone, output streams from all proposed configurations are the remaining fermentation broth (containing most of the water, microorganisms and other nonvolatile components) and two high-purity water streams. These streams may be recycled to the fermentation. Therefore, the value of the material intensity metric for all designed recovery processes is equal to zero. A more detailed insight should be obtained with reliable data for the fermentation process.[25,50]
- *Greenhouse gas emission*: CO_2 emission is the highest for PTD-MED both in the case of using green (0.191 kg_{CO2} $kg_{IPA+AC}{}^{-1}$) and grey (0.342 kg_{CO2} $kg_{IPA+AC}{}^{-1}$) electricity. This is due to the significantly higher heating requirements, originating from the multi-effect distillation in PTD-MED.
- *Pollution and toxic materials*: Values of these sustainability metrics are zero since pollutants (besides the already described CO_2) and toxic materials are not emitted.

CONCLUSIONS

The results of this original research can substantially contribute to the scale-up of isopropanol and acetone production by syngas fermentation. Novel industrial-scale (production capacity 100 kt_{IPA+AC} y^{-1}) vacuum distillation and pass-through distillation processes, in combination with regular atmospheric distillation and extractive distillation, were successfully designed. High-purity isopropanol and acetone (each 99.8 wt%) products can be obtained with recoveries of more than 99.2%, while allowing full recycling of biomass and water to enhance the upstream fermentation process. The implemented advanced heat pumping and heat integration significantly minimize the energy requirements and reduce CO_2 emission. As all three processes are highly competitive (cost of 0.109–0.137 USD $kg_{IPA+AC}{}^{-1}$, and energy use of 1.348–2.043 kW_{th} h $kg_{IPA+AC}{}^{-1}$), the exact configuration should be chosen depending on the plant location. By proposing three cost-effective and energy-efficient downstream process designs, this unique research presents a major step toward the expansion of industrial fermentation technology as an alternative to conventional fossil fuel-based processes.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

REFERENCES

1 Kiss AA, Grievink J and Rito-Palomares M, A systems engineering perspective on process integration in industrial biotechnology. *J Chem Technol Biotechnol* **90**:349–355 (2015).

2 Liew FE, Nogle R, Abdalla T, Rasor BJ, Canter C, Jensen RO *et al*., Carbon-negative production of acetone and isopropanol by gas fermentation at industrial pilot scale. *Nat Biotechnol* **40**:335–344 (2022).

3 Yang H, Zhang C, Lai N, Huang B, Fei P, Ding D *et al*., Efficient isopropanol biosynthesis by engineered Escherichia coli using biologically produced acetate from syngas fermentation. *Bioresour Technol* **296**:122337 (2020).

4 Ko YJ, Cha J, Jeong WY, Lee ME, Cho BH, Nisha B *et al*., Bio-isopropanol production in Corynebacterium glutamicum: Metabolic redesign of synthetic bypasses and two-stage fermentation with gas stripping. *Bioresour Technol* **354**:127171 (2022).

5 Molitor B, Richter H, Martin ME, Jensen RO, Juminaga A, Mihalcea C *et al*., Carbon recovery by fermentation of CO-rich off gases - Turning steel mills into biorefineries. *Bioresour Technol* **215**:386–396 (2016).

6 Liu L, Yang J, Yang Y, Luo L, Wang R, Zhang Y *et al*., Consolidated bioprocessing performance of bacterial consortium EMSD5 on hemicellulose for isopropanol production. *Bioresour Technol* **292**:121965 (2019).

7 Simpson SD, Koepke M, Liew F and Chen WY, Recombinant microorganisms and uses thereof WO 2012/115527 A2 (2012).

8 Arslan K, Schoch T, Höfele F, Herrschaft S, Oberlies C, Bengelsdorf F *et al*., Engineering Acetobacterium woodii for the production of isopropanol and acetone from carbon dioxide and hydrogen. *Biotechnol J* **17**:1–12 (2022).

9 Ramachandriya KD, Wilkins MR, Delorme MJM, Zhu X, Kundiyana DK, Atiyeh HK *et al*., Reduction of acetone to isopropanol using producer gas fermenting microbes. *Biotechnol Bioeng* **108**:2330–2338 (2011).

10 Jojima T, Inui M and Yukawa H, Production of isopropanol by metabolically engineered Escherichia coli. *Appl Microbiol Biotechnol* **77**: 1219–1224 (2008).

11 LanzaTech, *Closing the Carbon Cycle and Creating a Pathway to Net-Zero* (2022). https://lanzatech.com/closing-the-carbon-cycle-and-creating-a-pathway-to-net-zero (accessed 10 July 2023).

12 Straathof AJJ, Modelling of end-product inhibition in fermentation. *Biochem Eng J* **191**:108796 (2023).

13 Redl S, Sukumara S, Ploeger T, Wu L, Ølshøj Jensen T, Nielsen AT *et al*., Thermodynamics and economic feasibility of acetone production from syngas using the thermophilic production host Moorella thermoacetica. *Biotechnol Biofuels* **10**:1–17 (2017).

14 Panjapakkul W and El-Halwagi MM, Technoeconomic analysis of alternative pathways of isopropanol production. *ACS Sustain Chem Eng* **6**: 10260–10272 (2018).

15 Van Hoof V, Van den Abeele L, Buekenhoudt A, Dotremont C and Leysen R, Economic comparison between azeotropic distillation and different hybrid systems combining distillation with pervaporation for the dehydration of isopropanol. *Sep Purif Technol* **37**:33–49 (2004).

16 Daniell J, Köpke M and Simpson SD, Commercial biomass syngas fermentation. *Energies* **5**:5372–5417 (2012).

17 Janković T, Straathof AJJ and Kiss AA, Advanced downstream processing of bioethanol from syngas fermentation. *Sep Purif Technol* **322**:124320 (2023).

18 Koepke M, Simpson S, Liew F and Chen W, Fermentation process for producing isopropanol using a recombinant microorganisms US9365868B2 (2016).

19 Humbird D, Davis R, Tao L, Kinchin C, Hsu D, Aden A *et al*., *Process design and economics for biochemical conversion of lignocellulosic biomass to ethanol*. National Renewable Energy Laboratory, Golden (2011).

20 Kiss AA, Design, control and economics of distillation, in *Advanced Distillation Technologies: Design, Control and Applications*. Wiley, Chichester, pp. 37–66 (2013).

21 Mantingh J and Kiss AA, Enhanced process for energy efficient extraction of 1,3-butadiene from a crude C4 cut. *Sep Purif Technol* **267**: 118656 (2021).

22 Schwarz J, Beloff B and Beaver E, Use sustainability metrics to guide decision-making. *Chem Eng Prog* **98**:58–63 (2002).

23 BP, Approximate conversion factors, in *Statistical Review of World Energy*. (2021). www.bp.com (accessed 15 June 2023).

24 Lieberman NP and Lieberman ET, Steam generation, in *A Working Guide to Process Equipment*. McGrawHill, New York, pp. 261–276 (2022).

25 Dicks AP and Hent A, *Green Chemistry Metrics, A Guide to Determining and Evaluating Process Greenness*. Springer, Jiapur (2015).

26 Kiss AA and Suszwalak DJPC, Innovative dimethyl ether synthesis in a reactive dividing-wall column. *Comput Chem Eng* **38**:74–81 (2012).

27 Aspen Technology, *Aspen Physical Property System*. Bedford (2020). https://www.aspentech.com

28 Sulzer, *Structured packings* (2023). https://www.sulzer.com/en/products/separation-technology/structured-packings (accessed 10 May 2023).

29 Kiss AA, Distillation technology-still young and full of breakthrough opportunities. *J Chem Technol Biotechnol* **89**:479–498 (2014).

30 Kiss AA and Infante Ferreira CA, Mechanically driven heat pumps, in *Heat Pumps in Chemical Process Industry*. CRC Press, Boca Raton, pp. 189–251 (2016).

31 Kiss AA, McGregor IR and Furlong S, Pass-through distillation-a new player in separation technology. *NPT Procestechnologie* **1404**: 16–17 (2014).

32 McGregor I and Furlong S, Concurrent alcohol recovery and fermentation using pass-through distillation. *Ind Biotechnol* **13**: 107–112 (2017).

33 McGregor IR and Belchers CH, Stripping absorption module US8757599 B2 (2014).

34 Lin Y, ten Kate A, Moojier M, Deldago J, Fosbal PL and Thomsen K, Comparison of activity coefficient models for electrolyte systems. *AIChE J* **56**:1334–1351 (2009).

35 Nasirzadeh K, Neueder R and Kunz W, Vapor pressures, osmotic and activity coefficients of electrolytes in protic solvents at different temperatures. 3. Lithium bromide in 2-propanol. *J Solution Chem* **34**:9–24 (2005).

36 Al-Sahhaf TA and Jabbar NJ, Vapor-liquid equilibrium of the acetone-water-salt system. *J Chem Eng* **38**:522–526 (1993).

37 Sada EZO, Ohno T and Kito S, Salt effect on vapor-liquid equilibria for acetone-water system. *J Chem Eng Jpn* **5**:215–218 (1972).

38 Patil KR, Trlpathi AD, Pathak G and Katti SS, Thermodynamic properties of aqueous electrolyte solutions. 1. Vapor pressure of aqueous solutions of LiCl, LiBr and LiI. *J Chem Eng Data* **35**: 166–168 (1990).

39 Cui Y, Zhang Z, Shi X, Guang C and Gao J, Triple-column side-stream extractive distillation optimization via simulated annealing for the benzene/isopropanol/water separation. *Sep Purif Technol* **236**: 116303 (2020).

40 Li Y, Ye Q, Wang N, Chen L, Zhang H and Xu Y, Energy-efficient extractive distillation combined with heat-integrated and intermediate reboilers for separating acetonitrile/isopropanol/water mixture. *Sep Purif Technol* **262**:118343 (2021).

41 Shan B, Zheng Q, Chen Z, Shen Y, Zhang F, Wang Y *et al*., Dynamic control and performance comparison of conventional and dividing wall extractive distillation for benzene/isopropanol/water separation. *J Taiwan Inst Chem Eng* **128**:73–86 (2021).

42 Liu X, Wu J, Lei Y, Wu X, Man Y, Luo H *et al*., Data-driven surrogate optimized and intensified extractive distillation process for clean separation of isopropanol from water: a sustainable alternative. *J Clean Prod* **383**:135475 (2023).

43 Lei Z, Zhang J and Chen B, Separation of aqueous isopropanol by reactive extractive distillation. *J Chem Technol Biotechnol* **77**:1251–1254 (2002).

44 Shan B, Niu C, Meng D, Zhao Q, Huo B, Ma Y *et al*., Dynamic control of heat pump assisted extractive distillation process for separation of ethyl acetate/isopropanol/water mixture. *J Chem Technol Biotechnol* **96**:2368–2381 (2021).

45 Volker E, *How to design and optimise sieve trays*. WelChem, Eichenau (2020).

46 Taylor F, Kurantz MJ, Goldberg N and Craig JC Jr, Effects of ethanol concentration and stripping temperature on continuous fermentation rate. *Appl Microbiol Biotechnol* **48**:311–316 (1997).

47 Cuellar MC and Straathof AJJ, Improving fermentation by product removal, in Intensification of Biobased Processes, *RSC Green Chemistry series. Royal Society of Chemistry*, United Kingdom, pp. 86–108 (2018).

48 Sundquist J, Blanch HW and Wilke CR, Vacuum fermentation, in *Extractive Bioconversions*. CRC Press, Boca Raton, pp. 237–258 (1990).

49 Straathof AJJ and Bampouli A, Potential of commodity chemicals to become bio-based according to maximum yields and petrochemical prices. *Biofuels Bioprod Biorefin* **11**:798–810 (2017).

50 Sheldon RA, Metrics of green chemistry and sustainability: past, present, and future. *Sustain Chem Eng* **6**:32–48 (2018).