On the Synthesis of Biorefineries for High-Yield Isobutanol Production: From Biomass-to-Alcohol Experiments to System Level Analysis

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Supporting Information

S.1. Experimental results

Table S1. Details of experimental results for GVL pretreatment, hydrolysis, and fermentation.

	Poplar	Sorghum	Switchgrass
Pretreatment			
Glucan content of untreated biomass	53.3%	47.9%	42.5%
Xylan content of untreated biomass	21.2%	28.3%	29.7%
Lignin content of untreated biomass	22.4%	20.4%	25.9%
Biomass loading for pretreatment [g]	150.0	150.0	150.0
Total pulp obtained [g]	86.5	112.5	112.0
Hydrolysis			
Glucan content of cellulose pulp	58.9%	52.5%	53.7%
Moisture content of cellulose pulp	9.04%	6.02%	6.88%
Pulp loading for hydrolysis [g]	6.53	7.09	7.00
Volume of hydrolysate obtained [mL]	30.0 ± 1.0	27.8 ± 1.9	28.2 ± 1.6
Glucose concentration in hydrolysate [g/L]	100.7 ± 5.0	113.7 ± 3.3	107.1 ± 3.9
Xylose concentration in hydrolysate [g/L]	4.5 ± 0.5	6.1 ± 0.6	5.4 ± 0.5
Hydrolysate Fermentation			
Initial glucose concentration [g/L]	51.4	57.7	54.4
Final glucose concentration [g/L]	0.02	1.91	0.04
Initial xylose concentration [g/L]	2.41	3.20	2.85
Final xylose concentration [g/L]	2.41	4.20	3.73
Isobutanol titer [g/L]	18.69	22.30	20.05
Ethanol titer [g/L]	0.19	0.26	0.25

S.2. Mass & carbon balances

The biorefinery has three major outlets for carbon: (1) isobutanol product, (2) CO_2 released during fermentation, and (3) CO_2 released in the flue gas of the combustor & boiler block. Note that biomass is a biogenic source of carbon, and thus, the emissions associated with burning the residues are offset by the carbon required to grow the biomass. Table S2 provides the estimated relative carbon flow of the biorefinery for each feedstock. The estimations assume a generic chemical formula for glucan, xylan, and lignin of $(C_6H_{10}O_5)_n$, $(C_5H_8O_4)_n$, and $C_{81}H_{92}O_{28}$, respectively.

Table S2. Carbon flow of the biorefinery.

	Poplar	Sorghum	Switchgrass
Feedstock	100%	100%	100%
Isobutanol product	13.9%	18.8%	16.6%
Fermentation	6.9%	9.2%	8.2%
Combustor & boiler flue gas	79.2%	72.0%	75.2%

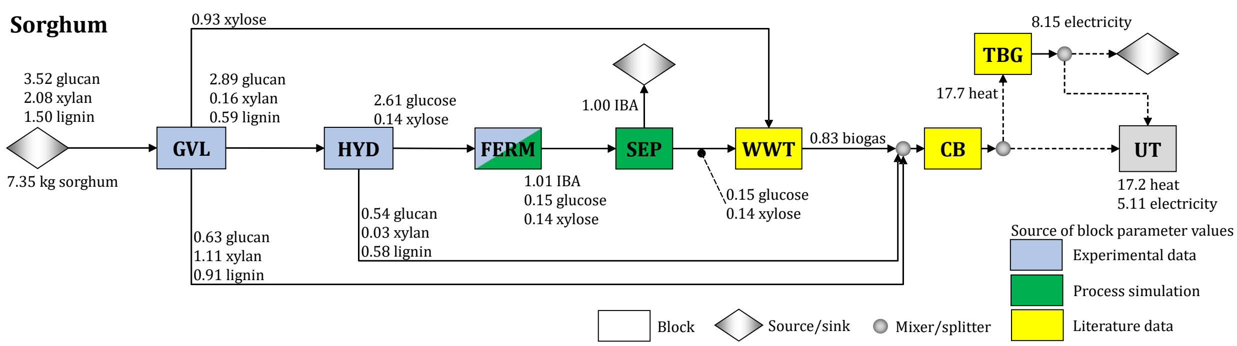

Figure S2. Block flow diagram of the baseline biomass-to-IBA biorefinery, using sorghum as feedstock. Mass flows are in units of kg kg^{-1} of IBA produced, and heat and electricity flows are in units of kWh kg^{-1} of IBA.

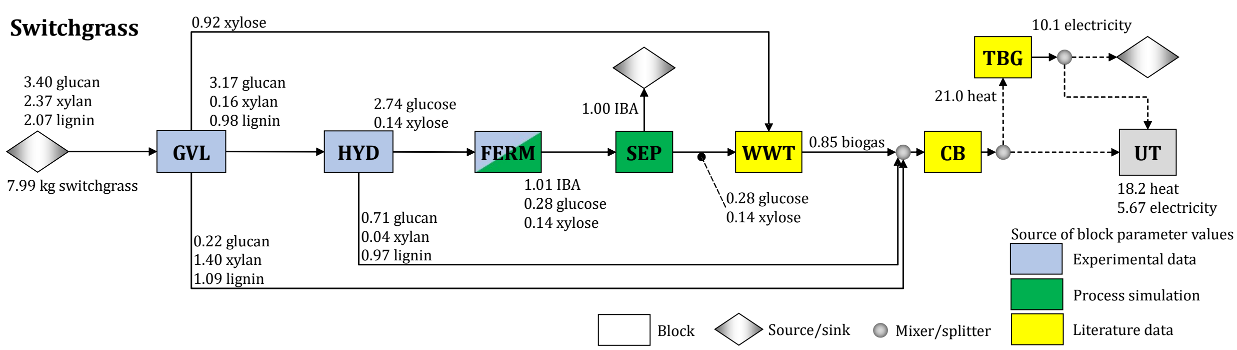

Figure S3. Block flow diagram of the baseline biomass-to-IBA biorefinery, using switchgrass as feedstock. Mass flows are in units of kg kg^{-1} of IBA produced, and heat and electricity flows are in units of kWh kg^{-1} of IBA.

S.3. Block parameters

In Section S.3.1, we show the values of block parameters used in the optimization model of the baseline biorefinery. In Section S.3.2, we describe the methodology to estimate these parameters for the different blocks.

S.3.1. Parameter values

The market price of biomass, natural gas, and electricity are shown in Table S3. The values of the cost and energy demand parameters of the baseline design are shown in Table S4. Finally, the values of the conversion parameters are shown in Table S5. All costs are indexed to 2017 US dollars.

Table S3. Market prices of biomass, natural gas, and electricity considered in this work.

Item	Price
Poplar[1]	$80.00/Mg
Sorghum[1]	$102.50/Mg
Switchgrass[1]	$101.00/Mg
Natural gas[2,3]	$0.600/kg
Electricity (purchase)[2,3]	$0.065/kWh
Electricity (export)[2,3]	$0.060/kWh

Table S4. Cost and energy demand parameters of blocks.

Block	Cost [$/kg or *$/kWh]	Heat demand [kWh/kg]	Electricity demand [kWh/kg]
GVL	0.149[a,b]	1.168	0.004
HYD[c]	0.434/0.399/0.371	0.358/0.316/0.295	1.086/1.012/0.947
FERM[a,d]	0.146	0.401	0.115
SEP[a,e]	0.025	6.345	0.011
WWT	0.008	0.0052	0.019
CB	0.060	–	0.058
TBG	*0.008	–	–

[a] Averages of the calculations from using the three biomass options.
[b] Deviation is 0.001 among the different biomass options.
[c] Values for the biorefinery using poplar/sorghum/switchgrass, respectively.
[d] Deviations for cost, heat demand, and electricity demand are 0.003, 0.036, and 0.001, respectively, among the different biomass options.
[e] Deviations for cost, heat demand, and electricity demand are 0.002, 0.470, and 0.001, respectively, among the different biomass options.

Table S5. Values for conversion parameters $\eta_{i,j,i',j'}$ and $\eta^{E}_{i,i',j}$, where i is the component being converted, i' is the product component, j is the block in which the conversion occurs, and j' is the block to which i' is sent to.

i	j	i'	j'	$\eta_{i,j,i',j'}$ or *$\eta^{E}_{i,i',j}$
POPLAR	SRC	GLUCAN	GVL	0.533
POPLAR	SRC	XYLAN	GVL	0.212
POPLAR	SRC	LIGNIN	GVL	0.224
SORGHUM	SRC	GLUCAN	GVL	0.479
SORGHUM	SRC	XYLAN	GVL	0.283
SORGHUM	SRC	LIGNIN	GVL	0.204
SWITCHGRASS	SRC	GLUCAN	GVL	0.425
SWITCHGRASS	SRC	XYLAN	GVL	0.297
SWITCHGRASS	SRC	LIGNIN	GVL	0.259
GLUCAN	GVL	GLUCAN	HYD	0.617/0.821/0.935[a]
XYLAN	GVL	XYLAN	HYD	0.069/0.075/0.067[a]
LIGNIN	GVL	LIGNIN	HYD	0.192/0.393/0.474[a]
GLUCAN	GVL	GLUCAN	CB	0.383/0.179/0.065[a]
XYLAN	GVL	XYLAN	CB	0.580/0.531/0.591[a]
LIGNIN	GVL	LIGNIN	CB	0.808/0.607/0.526[a]
XYLAN	GVL	XYLOSE	WWT	0.399/0.449/0.388[a]
GLUCAN	HYD	GLUCOSE	FERM	0.863/0.903/0.863[a]
XYLAN	HYD	XYLOSE	FERM	0.863/0.903/0.863[a]
GLUCAN	HYD	GLUCAN	CB	0.223/0.187/0.223[a]
XYLAN	HYD	XYLAN	CB	0.240/0.205/0.241[a]
LIGNIN	HYD	LIGNIN	CB	0.990
GLUCOSE	FERM	IBA	SEP	0.364/0.387/0.369[a]
GLUCOSE	FERM	GLUCOSE	SEP	0.115/0.059/0.103[a]
XYLOSE	FERM	XYLOSE	SEP	1.000
IBA	SEP	IBA	SNK	0.995
GLUCOSE	SEP	GLUCOSE	WWT	1.000
XYLOSE	SEP	XYLOSE	WWT	1.000
GLUCOSE	WWT	BIOGAS	CB	0.267
XYLOSE	WWT	BIOGAS	CB	0.733
BIOGAS	CB	HEAT	–	16.670*
GLUCAN	CB	HEAT	–	7.580*
XYLAN	CB	HEAT	–	7.580*
LIGNIN	CB	HEAT	–	8.200*
NG	CB	HEAT	–	13.880*
HEAT	TBG	ELEC	–	0.750*

[a] Values for the biorefinery using poplar/sorghum/switchgrass, respectively. Abbreviations – ELEC: electricity, IBA: isobutanol, NG: natural gas, SG: switchgrass, SNK: sink, SRC: source.

S.3.2. Parameter estimation

In Sections S.3.2.1 to S.3.2.3, we describe the estimation of cost and energy (heat and electricity) demand parameters for γ-valerolactone pretreatment (GVL), hydrolysis (HYD), and fermentation (FERM) and separation (SEP) blocks, respectively. The cost and energy demand parameters for the wastewater treatment (WWT), combustor and boiler (CB), and turbogenerator (TBG) blocks are estimated from papers on ethanol biorefinery.[4–6] The parameter calculations follow the procedure described by Pastore de Lima *et al.*[7] and consider a biorefinery that processes 2000 Mg/day of dry biomass. Table S6 shows the economic factors used for capital and operating costs.

Table S6. Economic factors used to determine costs.

Economic factor	**Value**
Equipment cost	100%
Indirect cost	
Engineering	32%
Construction	34%
Legal and contractors fees	23%
Project contingency	37%
Total indirect cost (TIC)	126%
Fixed operating costs	
Labor charge	2% of TDC
Overhead	60% of labor charge
Maintenance	7% of total equipment cost
General & administrative	5% of TDC
Tax & insurance	2% of capital cost
Capital cost	
Plant lifetime	25 years
Interest rate	10%
Capital recovery factor	0.1102
Variable operating cost	
Yearly hours of operation	8410 hr/yr

S.3.2.1. γ-valerolactone pretreatment

The GVL block consist of several sections (Figure S3). First, the biomass goes through biomass fractionation in which cellulose fibers and a liquid residue stream are obtained.[8] The liquid residue stream is rich in xylose and solubilized lignin. The lignin is separated from the liquid stream by using water to precipitate lignin.[9] The solids are sent to the CB block and the liquid stream is sent to a GVL recovery section. The GVL recovery section uses toluene to extract the GVL.[9] Furthermore, the GVL recovery section includes a reactor to produce GVL from levulinic acid.[9] The GVL is recycled to the reactor section, and the xylose residue stream goes to the wastewater treatment, where it is converted into biogas for heat generation.

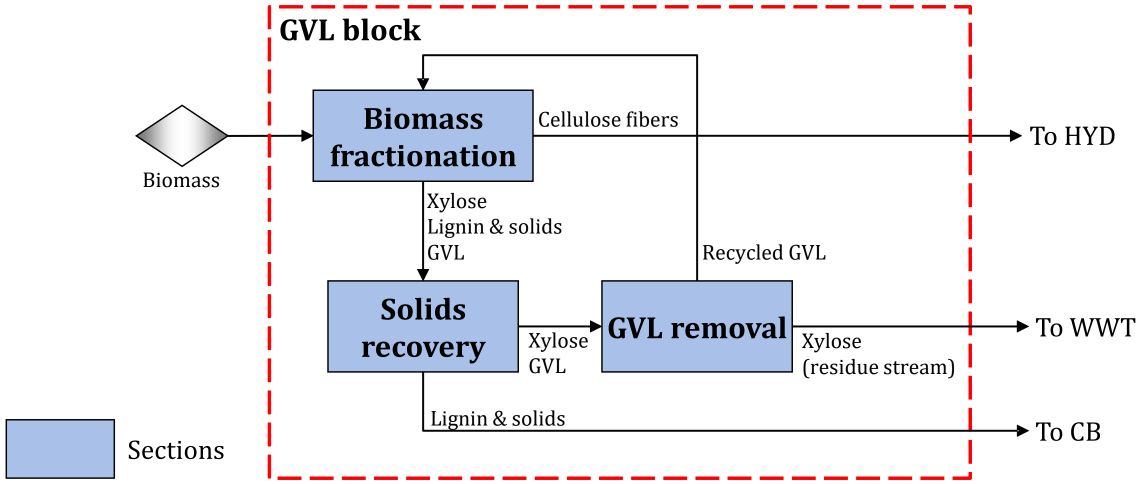

Figure S3. Details of the GVL block.

The conversion parameters of the GVL block are determined based on mass balance of the experimental data (Table S1), which are shown in Table S5. The cost and energy demand for the GVL block are estimated for each section of the GVL block. First, for each section, a scaling factor (SF) is determined based on the estimated inlet mass flow in the section divided by the inlet mass flow of the reference work. The energy (*i.e.*, heat and electricity) demands are calculated by scaling the original energy demands linearly with SF. The equipment (EC) and installed costs (IC) are calculated using Equation (S1),

$$C = \begin{cases} C_0 \times \lfloor SF \rfloor \times \left(\dfrac{SF}{\lfloor SF \rfloor}\right)^{\alpha}, & if\ SF \geq 2 \\ C_0 \times \left(\dfrac{SF}{\lceil SF \rceil}\right)^{\alpha}, & if\ SF < 2 \end{cases} \tag{S1}$$

where C_0 is the original (equipment or installed) cost, indexed to 2017 dollars, and α is the scaling exponent equals to 2/3.

Note that Equation (S1) considers that multiple identical units operate in parallel if $SF \geq 2$, which avoids designing units with large capacities. For instance, if $SF = 2.5$, then two identical units operate in parallel, where the capacity of each unit is 1.25 times larger than the capacity of the original unit. A list of the scaling factors, and equipment and installed costs for each section of the GVL block is shown in Table S7 for the biorefinery using sorghum.

Table S7. Detailed equipment and installed cost data of sections within the GVL block for the biorefinery using sorghum.

Unit	Scaling factor	Equip. cost	Installed cost
Biomass fractionation	2.77	$143,691,989	$217,822,746
Pulp bleaching[a]	1.46	$26,442,588	$26,442,588
Solids recovery	1.73	$18,870,841	$19,703,446
GVL recovery	1.84	$1,976,518	$3,707,368

[a] Part of the biomass fractionation section; scaling factor estimated from the flow of pulp to the pulp bleaching section.

The biomass fractionation section includes a pulp bleaching section.[8] The original work considers a GVL/biomass ratio of 1.63 kg/kg in the reactor. In our work, an experimental GVL/biomass ratio of 7.2 kg/kg is used. Therefore, the estimated is inlet mass flow considers the additional solvent mass flow required to achieve a GVL/biomass ratio of 7.2 kg/kg. Such additional solvent increases the flow in the solids and GVL recovery section, which are based on the alternative design proposed by Won *et al.*[9] Table S8 shows a summary of costs and energy demand for GVL.

Table S8. Summary of costs and energy demand of GVL pretreatment block for the biorefinery using sorghum.

Item	**Value**
Capital cost	
Equipment cost	$190,981,935
Installed cost	$267,676,148
Indirect cost	$240,637,239
Total capital cost	**$508,313,386**
Operating costs	
Raw materials	$3,541,713/yr
Cooling water demand	11463 kW
Cooling water cost	$457,393/yr
Variable operating costs	**$3,999,107/yr**
Fixed operating costs	**$45,484,447/yr**
Total annualized cost	**$105,483,460/yr**
Heat demand	97661.2 kW
Electricity demand	374.5 kW
Activity level	2000 Mg/day
Parameters	
Cost	$0.151/kg
Heat demand	1.172 kWh/kg
Electricity demand	0.004 kWh/kg

S.3.2.2. Hydrolysis

The cellulose fibers (from the GVL block) go through enzymatic hydrolysis to produce a hydrolysate rich in glucose, following the general reaction $(C_6H_{10}O_5)_n + n\,H_2O \rightarrow n\,C_6H_{12}O_6$. Then, the hydrolysate is filtrated to remove solids, which are sent to the combustor & boiler (CB block) for heat generation. The clean glucose stream is sent to fermentation (FERM block).

The cost and energy demand of the hydrolysis section are estimated from NREL reports[4,10,11] and includes the enzyme production section.[4] The calculations follow the procedure described by Pastore de Lima *et al.*[7] A scaling factor of 0.94 is determined based on the glucan present in the pulp and a glucan loading of 7%. Furthermore, a factor of 1.4 is introduced to account for the 7-day residence time (from 5-day residence time in the original reports[10,11]). Note that the enzymes production section is not scaled based on the residence time; instead, the variable costs such as the purchase of auxiliary materials (e.g., corn steep liquor used for enzyme production), equipment and installed costs, and energy demand are scaled based on the enzyme produced. In the original work,[4] 23.7 mg protein/g cellulose is used (620 kg/hr or protein produced), whereas 133 mg/g cellulose is used in this work, which corresponds to 4360 kg/hr of protein required. Therefore, an enzyme scaling factor of 7.04 is applied. A scaling exponent of 2/3 is used to determine the equipment and installed costs, while the energy demand and variable operating costs scale linearly.

The filtration section is based on the design proposed by Humbird *et al.*[4] The scaling factor is based on the estimated flow of solids (e.g., lignin) after hydrolysis of the pulp.

Table S9. Detailed cost data of different sections within the HYD block for a biorefinery using sorghum.

Unit ID	Hydrolysis	Enzyme production	Filtration
Equipment cost	$17,981,141	$42,594,323	$4,759,848
Installed cost	$21,857,257	$72,736,425	$8,228,931
Raw materials cost [$/yr]	–	$97,510,137	–
CW cost [$/yr]	$689,995	$3,179,962	$36,384
Heat demand [kW]	9653	3386	–
Electricity demand [kW]	2898	37579	1281

Table S10. Summary of costs and energy demand for hydrolysis for the biorefinery using sorghum.

Item	Value
Capital cost	
Equipment cost	$65,335,312
Installed cost	$102,822,613
Indirect cost	$82,322,494
Total capital cost	**$185,145,106**
Operating costs	
Raw materials	$97,510,137/yr
Cooling water demand	97900 kW
Cooling water cost	$3,906,340/yr
Variable operating costs	**$101,416,478/yr**
Fixed operating costs	**$16,707,828/yr**
Total annualized cost	**$138,521,385/yr**
Heat demand	13039 kW
Electricity demand	41758 kW
Activity level	41252 kg/hr
Parameters	
Cost	$0.399/kg
Heat demand	0.316 kWh/kg
Electricity demand	1.012 kWh/kg

S.3.2.3. Fermentation and isobutanol recovery

We simulate the fermentation and alcohol recovery processes using Aspen Plus (Aspen Tech V11) to estimate the baseline cost and energy demand parameters for the FERM and SEP blocks in the optimization model, as well as the conversion parameters for isobutanol recovery. The NRTL-RK thermodynamic package is used, with exception of the vacuum flash unit, which uses the WILSON thermodynamic package to model the vapor–liquid equilibrium under vacuum. The process simulation is shown in Figure 5 (Section 4.4). During fermentation, the glucose produces isobutanol following the fermentation reaction $C_6H_{12}O_6 \rightarrow C_4H_9OH + 2CO_2 + H_2O$. The parameter calculation follows the procedure described by Pastore de Lima *et al.*[7] Table S11 shows the detailed costs obtained from APEA or literature estimations[4] for each unit, using sorghum as feedstock. Table S12 summarizes the cost and energy demand of the fermentation and separation blocks.

Table S11. Detailed cost information of FERM and SEP unit operations for the biorefinery using sorghum.

Unit*	Equip. cost	Installed cost	Var. oper. Cost ($/yr)
Bioreactor[a]	$14,960,071	$24,519,477	$3,639,688
V-101	$625,558	$3,106,336	
P-101	$115,175	$846,874	
C-101	$37,042,290	$44,318,635	
H-101	$199,862	$1,095,291	$489,706
V-102	$455,054	$2,076,536	
P-102	$63,233	$405,371	
C-102	$10,614,160	$13,415,621	
H-102	$134,371	$901,074	$140,389
D-201	$44,696	$196,004	$13,321
H-201	$14,679	$94,285	
H-202	$18,914	$108,588	$20,036
H-203	$78,759	$226,774	
H-204	$25,124	$115,457	$80,863
COL-201	$387,304	$1,085,693	$160,262
COL-202	$681,922	$1,753,783	$903,087

* Units shown in Figure 5 (Section 4.4).

[a] Estimated from Humbird et al.[4]

Table S12. Summary of costs and energy demand of FERM and SEP blocks for the biorefinery using sorghum.

Item	FERM	SEP
Capital cost		
Equipment cost	$64,209,774	$1,251,398
Installed cost	$90,685,215	$3,580,585
Indirect cost	$80,904,315	$1,576,762
Total capital cost	**$171,589,531**	**$5,157,347**
Operating costs		
Auxiliary materials	$2,674,145/yr	–
Cooling water	$965,543/yr	$1,177,569/yr
Variable operating costs	**$3,639,688/yr**	**$1,177,569/yr**
Fixed operating costs	**$15,362,662/yr**	**$484,353/yr**
Total annualized cost	**$37,906,038/yr**	**$2,230,097/yr**
Heat demand	14269 kW	66805 kW
Electricity demand	3675.1 kW	109.4 kW
Activity level	31713 kg/hr	11633 kg/hr
Parameters		
Cost	$0.142/kg	$0.023/kg
Heat demand	0.450 kWh/kg	5.743 kWh/kg
Electricity demand	0.116 kWh/kg	0.009 kWh/kg

S.4. Optimization model

In this Section, we present the formal problem statement and the model formulation of the biorefinery, adapted from Pastore de Lima *et al.*[7]

S.4.1. Problem statement

We are given a set of components $i \in I$ that include the feedstocks I^F (*i.e.*, poplar, sorghum, and switchgrass), products I^P (*i.e.*, isobutanol), intermediates I^I (*e.g.*, glucan, glucose, lignin, biogas), resources I^R (*i.e.*, natural gas), and energy I^E (*i.e.*, heat and electricity), where the price of feedstock, resources, and energy are known. We are also given a set of blocks $j \in J$ that includes source ($j = SRC$), sink ($j = SNK$), and technology blocks ($j \in J^T$). The technology blocks convert components (*e.g.*, intermediates) into other components (*e.g.*, products) or energy (*e.g.*, heat). They are characterized by cost (γ_j, [\$/kg]), energy demand ($\lambda_{i,j}$, [kWh/kg]), and conversion ($\eta_{i,j,i',j'}$, [kg i'/kg i]) parameters that are used to calculate the total cost, total energy demand, and the outlet component flows of the block ($F_{i,j,j'}$), respectively. The values of the block parameters are known (see Section S.3.1). The goal is to minimize the total cost to meet a demand of 1 kg of isobutanol.

We introduce the following sets, parameters, and variables.

Sets

I^S	Solid components (*i.e.*, glucan, xylan, and lignin)
I^A_j	Components used to calculate the activity level of block j
$I_{j,j'}$	Components present in stream from block j to block j'
J^{TBG}	Turbogenerator block
J^{CB}	Combustor and boiler block
J^{WWT}	Wastewater treatment block
$J^{IN/OUT}_j$	Blocks that have streams to/from block j
$J^{IN}_{i,j}$	Blocks that have a stream to block j and component i is present in the stream, *i.e.*, $J^{IN}_{i,j} = \left\{ j' \in J^{IN}_j \mid j \in J, i \in I_{j',j} \right\}$

Parameters

δ	Total demand of isobutanol, [kg]
$\eta^E_{i,j,i'}$	Conversion of component i to energy i' in block j, [kWh i'/kg i]
π^P_i/π^S_i	Component i purchase/sell price, [\$/kg]
κ	Boiler efficiency
ω^{sugar}	Mass fraction of sugars (*i.e.*, glucose and xylose) in the hydrolysate
ϕ_{IBA}	Conversion factor of mass of IBA to gallon gasoline equivalent (GGE), [GGE/kg]

Variables

A_j	Activity level of block j
$E_{i,j,j'}$	Flow of energy i from block j to block j'
E^{UT}_i	Total demand of energy i in the biorefinery

E^W	Waste heat from combustor and boiler
$E^{OUT}_{i,j}$	Flow of energy i out of block j
$F^{IN}_{i,j}$	Mass flow of component i into block j
F^{EXT}_{i}	Externally purchased mass flow of i
F^{SNK}_{i}	Mass flow of component i in the sink

S.4.2. Mass balance

The inlet of a block is modeled as a mixer,

$$F^{IN}_{i,j} = \sum_{j' \in J^{IN}_{i,j}} F_{i,j',j},\ i \in I^I, j \in J^T \backslash J^{TBG} \tag{S2}$$

In a technology block, component i is converted to i', which is sent to block j', based on conversion parameter $\eta_{i,j,i',j'}$, except for combustor and boiler, and turbogenerator blocks,

$$F_{i,j,j'} = \sum_{i' \in I^I} \eta_{i',j',i,j} F^{IN}_{i',j},\ j \in J^T \backslash (J^{TBG} \cup J^{CB}), j' \in J^{OUT}_{j}, i \in I^I \cap I_{j',j} \tag{S3}$$

Non-technology blocks, such as the source and the sink are treated differently. Feedstock $i \in I^F$ is converted into its major components (*i.e.*, $I^S = \{GLUCAN, XYLAN, LIGNIN\}$) when sent to the GVL block from the source,

$$F_{i',j=SRC,j'=GVL} = \eta_{i,j=SRC,i',j'=GVL} F^{IN}_{i,j=SRC},\ i \in I^F, i' \in I^S \tag{S4}$$

Note that $F^{IN}_{i,j=SRC}$ is the mass flow of purchased feedstock i and $\eta_{i,j=SRC,i',j'=GVL}$ is the composition of the feedstock.

Sinks are modeled as mixers,

$$F^{SNK}_{i} = \sum_{j' \in J^{IN}_{i,j=SNK}} F_{i,j',j=SNK},\ i \in I^P \tag{S5}$$

The biorefinery must meet a demand for isobutanol,

$$\sum_{i \in I^P} F^{SNK}_{i} = \delta \tag{S6}$$

External resources (*i.e.*, natural gas) can be purchased and fed to the combustor block,

$$F^{EXT}_{i} = \sum_{j \in J^{CB}} F^{IN}_{i,j},\ i \in I^R \tag{S7}$$

S.4.3. Energy balance

Heat ($i = HEAT$) is produced in combustor and boiler blocks,

$$E^{OUT}_{i'=HEAT,j} = \kappa \sum_{i \in I^I \cup I^R} \eta^{E}_{i,i'=HEAT,j} F^{IN}_{i,j},\ j \in J^{CB} \tag{S8}$$

where the boiler efficiency is $\kappa = 0.8$.

The heat balance of the biorefinery is,

$$\sum_{j \in J^{CB}} E^{OUT}_{i = HEAT,j} = E^{UT}_{i = HEAT} + E^{W} + \sum_{j \in J^{CB}} \sum_{j' \in J^{OUT}_{j}} E_{i = HEAT,j,j'} \tag{S9}$$

The energy demand of the biorefinery is,

$$E^{UT}_{i} = \sum_{j \in J^{T}} \lambda_{i,j} A_j, \ i \in I^{E} \tag{S10}$$

where the activity level (A_j) is defined in Section S.4.4.

The electricity ($i = ELEC$) generated by a turbogenerator is given as,

$$E^{OUT}_{i = ELEC,j} = \eta^{E}_{i' = HEAT,i = ELEC,j} \sum_{j' \in J^{CB}} E_{i' = HEAT,j',j}, \ j \in J^{TBG} \tag{S11}$$

The electricity balance of the biorefinery is,

$$E^{EXT}_{i = ELEC} + \sum_{j \in J^{TBG}} E^{OUT}_{i = ELEC,j} = E^{UT}_{i = ELEC} + E^{SNK}_{i = ELEC} \tag{S12}$$

where E^{EXT}_{i} (E^{SNK}_{i}) is the electricity purchased (sold) from (to) the grid.

S.4.4. Activity level

The activity level A_j indicates the mass flow of material processed by a technology block. The activity level is a function of the block inlet mass flow,

$$A_j = \sum_{i \in I^{A}_{j}} F^{IN}_{i,j}, \ j \in J^{T} \setminus J^{WWT} \tag{S13}$$

Table S13 shows the components used to calculate A_j (*i.e.*, the elements of sets I^{A}_{j}).

Table S13. Components used to calculate the activity level of blocks.

Block	I^{A}_{j}
FERM	{GLUCOSE, XYLOSE}
SEP	$I^{P} = \{IBA\}$
TBG	$I^{E} = \{HEAT, ELEC\}$
Others*	$I \setminus I^{E}$

* Except WWT block

The activity level of the wastewater treatment block is based on the estimated water flow,

$$A_{j = WWT} = \left(\frac{1}{\omega^{sugar}} - 1\right) A_{j = FERM} \tag{S14}$$

where ω^{sugar} is the mass fraction of sugars (*i.e.*, glucose and xylose) in the hydrolysate, which is estimated based on the sugar concentration assuming a density of 1000 g/L for the hydrolysate.

S.4.5. Objective function

We minimize the costs to produce one kg of alcohol (isobutanol + ethanol),

$$Cost = \sum_{i \in I^F} \pi_i^P F_{i,j = SRC}^{IN} + \sum_{j \in J^T} \gamma_j A_j + \sum_{i \in I^R} \pi_i^P F_i^{EXT} + \sum_{i \in I^E} \left(\pi_i^P E_i^{EXT} - \pi_i^S E_i^{SNK} \right) \tag{S15}$$

where the first term on the RHS is the feedstock purchasing cost; the second term is the block costs; the third term is the purchasing cost of external resources (natural gas); the fourth term is the purchasing cost or revenues from electricity.

S.4.6. Minimum fuel selling price

In this work, we determine the minimum fuel selling price (MFSP) on a gasoline gallon equivalent (GGE). The flow of produced isobutanol is converted into a GGE flow, where the MFSP is determined by,

$$MFSP = \frac{Cost}{\phi_{IBA} F_{IBA}^{SNK}} \tag{S16}$$

where $\phi_{IBA} = 0.2752$ GGE/kg.

S.5. Sensitivity analysis

Sensitivity analysis is carried out using a new set of parameter values in the process optimization model for each studied case. The new set of block parameters are estimated by considering one or multiple improvements following the procedure described in Section S.3.2. The improvements are considered in the following parameters: (A) the GVL/dry biomass mass ratio during biomass fractionation, which is varied from 4.0 to 7.2 (increments of 0.05); (B) the enzyme loading during hydrolysis, varied from 19 to 133 mg protein/g of cellulose (increments of 2 mg protein/g of cellulose); (C) the cost parameter of the FERM block, varied from 40% to 100% of the baseline value (increments of 2%); and (D) the heat demand parameter of the SEP block, varied from 40% to 100% of the baseline value (increments of 2%).

For the cases where improvements (A) and (B) are considered, the cost and energy demand parameters of the GVL and HYD blocks are first determined over a wide range of GVL/biomass ratios and enzyme loadings, respectively. Then, functions are fitted to the obtained data. The functions are used in the optimization model to determine the block parameters in each instance of the optimization problem. Table S14 shows the functions used for each block parameter estimation.

Table S14. Functions obtained to calculate the cost and energy demand parameters of the GVL and HYD blocks as functions of the GVL/biomass mass ratio and enzyme loading, respectively. X: GVL/biomass mass ratio; Y: enzyme loading (mg protein/g cellulose).

	GVL block	**HYD block**
Cost parameter [$/kg]	$-0.0056X^2 + 0.081X - 0.1465$	$0.00267Y + 0.0472$
Heat demand parameter [kWh/kg]	$0.16277X$	$0.00062Y + 0.2340$
Electricity demand parameter [kWh/kg]	$0.00061X$	$0.00685Y + 0.1013$

References

1 C. H. Geissler and C. T. Maravelias, *Appl Energy*, 2021, **302**, 117539.

2 R. T. L. Ng, P. Fasahati, K. Huang and C. T. Maravelias, *Appl Energy*, 2019, **241**, 491–503.

3 K. Huang, P. Fasahati and C. T. Maravelias, *iScience*, 2020, **23**, 100751.

4 D. Humbird, R. Davis, L. Tao, C. Kinchin, D. Hsu, A. Aden, P. Schoen, J. Lukas, B. Olthof, M. Worley, D. Sexton and D. Dudgeon, *Process design and economics for conversion of lignocellulosic biomass to ethanol*, 2011.

5 R. T. L. Ng, P. Fasahati, K. Huang and C. T. Maravelias, *Appl Energy*, 2019, **241**, 491–503.

6 K. Huang, P. Fasahati and C. T. Maravelias, *iScience*, 2020, **23**, 100751.

7 A. E. Pastore de Lima, R. L. Wrobel, B. Paul, L. C. Anthony, T. K. Sato, Y. Zhang, C. T. Hittinger and C. T. Maravelias, *Sustainable Energy Fuels*, 2023, **7**, 3266–3275.

8 D. M. Alonso, S. H. Hakim, S. Zhou, W. Won, O. Hosseinaei, J. Tao, V. Garcia-Negron, A. H. Motagamwala, M. A. Mellmer, K. Huang, C. J. Houtman, N. Labbé, D. P. Harper, C. T. Maravelias, T. Runge and J. A. Dumesic, *Sci Adv*, 2017, **3**, e1603301.

9 W. Won, A. H. Motagamwala, J. A. Dumesic and C. T. Maravelias, *React. Chem. Eng.*, 2017, **2**, 397–405.

10 F. K. Kazi, J. Fortman, R. Anex, G. Kothandaraman, D. Hsu, A. Aden and A. Dutta, *Techno-Economic Analysis of Biochemical Scenarios for Production of Cellulosic Ethanol Techno-Economic Analysis of Biochemical Scenarios for Production of Cellulosic Ethanol*, Golden, Colorado, 2010.

11 A. Aden, M. Ruth, K. Ibsen, J. Jechura, K. Neeves, J. Sheehan, B. Wallace, L. Montague, A. Slayton and J. Lukas, *Lignocellulosic Biomass to Ethanol Process Design and Economics Utilizing Co-Current Dilute Acid Prehydrolysis and Enzymatic Hydrolysis for Corn Stover*, Golden, Colorado, 2002.