High Yield Co-production of Isobutanol and Ethanol from Switchgrass: Experiments, and Process Synthesis and Analysis

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Supplementary Information

S.1. Fermentation results of parent strains

Table S1. Titers (g/L) and yields (% of theoretical maximum) for major products from glucose consumed in Production Medium fermented anaerobically with BTX1858 in bioreactors for 48 h (N = 2, ± s.d.).

Product	Titer (g/L)	Yield (% of theoretical maximum)*
Isobutanol	15.37 ± 0.73	63.6% ± 3.3%
Ethanol	ND	NC
Glycerol	7.17 ± 0.44	NC

*Based on initial glucose concentration of 68.5 g/L. The final glucose concentration is 9.6 g/L ± 0.2 g/L (mean ± s.d.).
ND: not detected
NC: not calculated

Table S2. Titers (g/L) and yields (% of theoretical maximum) for major products from glucose consumed in AFEX-pretreated switchgrass hydrolysate (ASGH) fermented anaerobically with BTX1858 in bioreactors for 48 h (N = 3, ± s.d.).

Product	Titer (g/L)	Yield (% of theoretical maximum)*
Isobutanol	0.01 ± 0.02	NC
Ethanol	ND	NC
Glycerol	0.04 ± 0.01	NC

*Based on initial glucose concentration of 61 g/L and xylose concentration of 42 g/L. The final glucose concentration is 62 g/L ± 2 g/L and xylose concentration is 43 g/L ± 2 g/L (mean ± s.d.).
ND: not detected
NC: not calculated

Table S3. Titers (g/L) and yields (% of theoretical maximum) for major products from glucose and xylose consumed in AFEX-pretreated switchgrass hydrolysate (ASGH) fermented anaerobically with GLBRCY945 in bioreactors for 48 h (N = 6, ± s.d.).

Product	Titer (g/L)	Yield (% of theoretical maximum)*
Isobutanol	ND	NC
Ethanol	30.63 ± 3.64	81.3% ± 2.6%
Glycerol	3.50 ± 0.10	NC

*Based on initial glucose concentration of 52 g/L and xylose concentration of 40 g/L. The final glucose concentration is 0.01 g/L ± 0.02 g/L and xylose concentration of 19 g/L ± 8 g/L (mean ± s.d.).
ND: not detected
NC: not calculated

S.2. Block parameters

In Section S.2.1, we show the values of block parameters used in the optimization model of the baseline biorefinery. In Section S.2.2, we describe the methodology to estimate these parameters for the different blocks.

S.2.1. Parameter values

The market price of switchgrass, natural gas, and electricity are shown in Table S4. The values of the cost and energy demand parameters of the baseline design are shown in Table S5. Finally, the values of the conversion parameters are shown in Table S6. All costs are indexed to 2017 US dollars.

Table S4. Market prices of switchgrass, natural gas, and electricity considered in this work.

Item	Price
Switchgrass	\$0.101/kg
Natural gas	\$0.600/kg
Electricity (purchase)	\$0.065/kWh
Electricity (export)	\$0.060/kWh

Table S5. Cost and energy demand parameters of blocks.

Block	Cost [\$/kg or *\$/kWh]	Heat demand [kWh/kg]	Electricity demand [kWh/kg]
AFEX	0.034	0.665	0.035
HYD	0.155	0.142	0.379
FERM	0.029	–	0.040
SEP	0.100	8.903	0.071
FILT	0.027	–	0.097
WWT	0.00583	5.83×10^{-5}	0.027
CB	0.060	–	0.058
TBG	*0.008	–	–

Table S6. 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 $^*\eta^{E}_{i,i',j}$
SG	SRC	GLUCAN	AFEX	0.341[a]
SG	SRC	XYLAN	AFEX	0.270[a]
SG	SRC	LIGNIN	AFEX	0.264[a]
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*
GLUCAN	AFEX	GLUCAN	HYD	0.950
XYLAN	AFEX	XYLAN	HYD	0.950
LIGNIN	AFEX	LIGNIN	HYD	0.950
GLUCAN	HYD	GLUCOSE	FERM	0.8459
GLUCAN	HYD	GLUCAN	FERM	0.100
XYLAN	HYD	XYLAN	FERM	0.100
XYLAN	HYD	XYLOSE	FERM	0.7491
LIGNIN	HYD	LIGNIN	FERM	1.000
HEAT	TBG	ELEC	–	0.750*
GLUCAN	FERM	GLUCAN	SEP	0.990
XYLAN	FERM	XYLAN	SEP	0.990
LIGNIN	FERM	LIGNIN	SEP	1.000
GLUCAN	FILT	GLUCAN	CB	0.980
XYLAN	FILT	XYLAN	CB	0.980
LIGNIN	FILT	LIGNIN	CB	0.980
GLUCOSE	FILT	GLUCOSE	WWT	0.960
XYLOSE	FILT	XYLOSE	WWT	0.960
iBuOH	SEP	iBuOH	SNK	0.995
EtOH	SEP	EtOH	SNK	0.973
GLUCOSE	SEP	GLUCOSE	FILT	1.000
XYLOSE	SEP	XYLOSE	FILT	1.000
GLUCAN	SEP	GLUCAN	FILT	0.990
XYLAN	SEP	XYLAN	FILT	0.990
LIGNIN	SEP	LIGNIN	FILT	1.000

[a] Obtained from the base case in Laser et al.[1]
Abbreviations – ELEC: electricity, EtOH: ethanol, iBuOH: isobutanol, NG: natural gas, SG: switchgrass, SNK: sink, SRC: source.

S.2.2. Parameter estimation

Each block may represent different unit operations simultaneously (Figure S1). In Sections S.2.2.1 to S.2.2.3, we describe the estimation for cost and energy (heat and electricity) demand parameters for ammonia fiber expansion (AFEX), hydrolysis (HYD), and fermentation (FERM) and separation (SEP) blocks respectively. The cost and energy demand parameters for the filtration (FILT), wastewater treatment (WWT), combustor and boiler (CB), and turbogenerator (TBG) blocks are estimated from papers on ethanol biorefinery.[2,3]

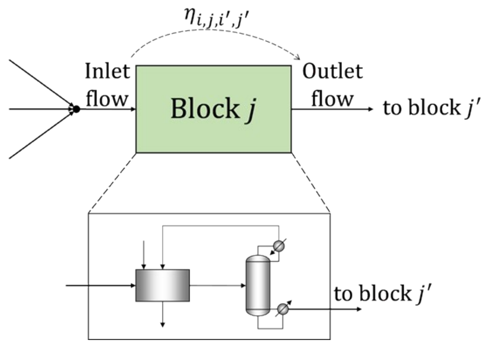

Figure S1. Block representing two unit operations.

The cost parameter includes the annualized capital cost plus the fixed and variable costs to operate the units corresponding to the block. The total capital cost is determined by the sum of total direct costs (TDC) and total indirect costs (TIC). Direct costs (*i.e.*, installed costs) and equipment costs for each unit are estimated from the literature or from detailed process simulations. Indirect costs (*e.g.*, construction, fees, project contingency) and fixed operating costs are determined based on the economic factors shown in Table S7. Variable operating costs are estimated using material flows (*e.g.*, auxiliary inputs such as make-up ammonia) and cooling water demand. Finally, the cost parameter is calculated by the sum of the total annualized capital cost and operating costs, divided by the inlet mass flow of a subset of components processed by the block (termed as the *activity level* of the block, see Section S.3.4 for details and the components used to determine the activity level of each block).

The electricity and heat demand parameters are calculated following a similar procedure. The total demand for heat (electricity) of a block is estimated by the sum of the heat (electricity) consumed by each unit operation. The parameter is calculated by dividing the total heat (electricity) demand by the activity level. Note that heat and electricity demands are not considered in the calculation of the cost parameters.

Table S7. 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.2.2.1. Ammonia fiber expansion pretreatment

The conversion parameters of the AFEX block are taken from the literature.[2,3] The cost and energy demand parameters are estimated using results from the design proposed by Laser et al.[1] We use the equipment and installed costs, and energy demand of the AFEX design (mature case with Rankine power).[1] The original work considers the processing of 4535 Mg/day of dry switchgrass, where AFEX uses a ratio of 0.3 kg of NH_3/kg of dry biomass into the AFEX reactor (residence time of 10 min). To re-estimate the equipment and installed costs of units, we scale the flows into each unit considering three major adaptations. First, all flows are scaled to a biorefinery processing 2000 Mg/day of dry switchgrass (scaling factor of 0.441 for all streams); energy demand is scaled similarly. Second, the ammonia flows are scaled considering a ratio of 1.0 kg of NH_3/kg of dry biomass in the AFEX reactor, which is consistent with the experiments conducted in this work. Thus, the flow of recycled NH_3 solution increases by a scaling factor of 3.33. We estimate the make-up flow of NH_3 as the sum of ammonia required to neutralize the acetate present in the switchgrass plus the ammonia lost in the stripping column. We consider the same ammonia recovery factor from the original work, 99.46%.[1] Energy demand increases by the scaling factor of 3.33 to account for the additional heat and electricity required to operate the unit operations recycling the ammonia. Third, we use an AFEX reactor three times larger to account for the increased residence time of 30 min. These adjustments result in the overall scaling factors (OSF) shown in Table S8 for each unit operation. The OSF is determined by the ratio of the scaled flow to the original flow reported by Laser et al.[1] (except for the

AFEX reactor, which has its OSF increased three-fold due to higher residence time, as mentioned above).

The equipment cost (EC) is determined by the following equation,

$$EC = EC_0 \times OSF^{\alpha} \quad \text{(S1)}$$

where EC_0 is the original equipment cost (indexed to 2017 dollars) and α is the scaling exponent.

The installed cost of equipment is determined by multiplying the equipment cost by an installation factor. A list of the overall scaling factor, scaling exponent, installation factor, equipment cost, and the installed cost is shown in Table S8.

Table S8. Detailed cost data of unit operations in AFEX.

Unit*	Reference stream*	Overall scaling factor	Scaling exp.*	Inst. factor*	Equip. cost	Installed cost
Cooling water condenser	QNH3-CW	1.470[a]	0.68	2.10	$537,998	$1,129,796
Chilled water condenser	QNH3-CHL	1.470[a]	0.68	2.10	$334,385	$702,208
Quench water mixer	F703	1.470[a]	0.71	2.80	$30,954	$86,670
Recycle pump	F703C	1.470[a]	0.70	2.80	$36,670	$102,675
NH_3 Feed Pump	F701	1.470[a]	0.70	2.80	$1,923	$5,384
Make-up Water Pump	F702	1.470[a]	0.79	2.50	$31,477	$78,693
AFEX Reactor	F201B	2.264[a,b,c]	0.80	2.29	$18,088,339	$41,422,297
NH_3 stripping column	F202A	0.755[a,b]	0.68	3.00	$2,007,111	$6,021,332
Slurry mixer	301	0.441[d]	0.71	2.80	$80,053	$224,149
Slurry agitator	301	0.441[d]	0.51	1.30	$331,141	$430,483
NH_3 day tank	F201A	1.470[a]	0.71	2.80	$661,737	$1,852,865

* From Laser et al.[1]
[a] Stream flows scaled by 0.441 and 3.33 scaling factors (biomass consumption basis and additional NH_3 solution).
[b] The presence of other components in the inlet stream (*e.g.*, biomass) reduces the overall scaling factor because only the NH_3 solution flow increases by the 3.33 scaling factor.
[c] The reactor overall scaling factor is multiplied by 3 to account for the 3-fold increase in residence time.
[d] The NH_3 scaling factor has a negligible effect on the total flow into the slurry mixer.

Table S9 shows a summary of costs and energy demand for AFEX. The total indirect costs and fixed operating costs are estimated using the economic factors in Table S7. Variable operating costs include NH_3 purchasing, and cooling water make-up and chemicals purchasing. The cost and energy parameters are determined by dividing the total costs and energy demand by the inlet flows of cellulose, hemicellulose, lignin, and soluble carbohydrates in the biomass stream to be consistent with the activity level used in the optimization model (see Section S.3.4).

Table S9. Summary of costs and energy demand of AFEX pretreatment.

Item	Value
Capital cost	
Equipment cost	$22,141,787
Installed cost	$52,056,551
Indirect cost	$27,898,652
Total capital cost	**$79,955,203**
Operating costs	
NH3 makeup	980.6 kg/hr
Ammonia price	$0.485/kg
Water make-up cost	$1,501,667/yr
CW chemicals cost	$100,111/yr
Variable operating costs	**$5,601,790/yr**
Fixed operating costs	**$7,417,666/yr**
Total annualized cost	**$21,827,967/yr**
Heat demand	50565 kW
Electricity demand	2654 kW
Activity level	75986 kg/hr
Parameters	
Cost	$0.034/kg
Heat demand	0.665 kWh/kg
Electricity demand	0.035 kWh/kg

S.2.2.2. Hydrolysis

The conversion parameters of the HYD block are adapted from the literature.[2,3] The original parameters may result in a glucose/xylose ratio in the hydrolysate slightly different than the ratio obtained in our hydrolysate. We adapt the conversion parameters of glucan to glucose and xylan to xylose to match the glucose/xylose ratio we obtain. The resulting parameters are shown in Table S6 (Section S.2.1).

The cost and energy demand parameters are estimated from NREL reports.[4–6] Equipment and installed cost data for the hydrolysis tanks and auxiliary unit operations are adapted from previous NREL reports[4,5] and are scaled to account for a 7-day residence time (from 5 days in the original reports). Heat and electricity demands are scaled linearly to account for a 7-day residence time. For a better estimation of the enzymes cost and the impact of the enzyme loading on the heat and electricity demands, we use the on-site enzyme production facility reported by Humbird et al.[6] 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 associated with this facility are scaled based on the enzyme loading. In the original work[6], 20 mg protein/g glucan is used, whereas 93 mg protein/g glucan is used in this work; therefore, an enzyme loading scaling factor of 4.65 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. Table S10 shows the list of equipment and installed costs of unit operations in the HYD block. The unit operations for on-site enzyme production are lumped in the unit ID "Area 400". Table S11 summarizes the costs and energy demand of the HYD block.

Table S10. Detailed cost data of unit operations in the HYD block.

Unit ID	Equipment cost	Installed cost
A-310[a]	$1,097,436	$1,316,923
H-301[a]	$104,961	$220,418
H-302[b]	$122,079	$256,366
H-310[a]	$6,612	$13,885
P-310[a]	$12,758	$35,722
T-310[a]	$13,477,286	$16,172,743
Area 400[c]	$32,313,384	$55,180,125

[a] From Kazi et al.[4]
[b] From Aden et al.[5]
[c] From Humbird et al.[6]

Table S11. Summary of costs and energy demand for hydrolysis.

Item	Value
Capital cost	
Equipment cost	$47,134,516
Installed cost	$73,196,183
Indirect cost	$59,389,490
Total capital cost	**$132,585,674**
Operating costs	
Glucose flow	11244 kg/hr
Corn steep liquor flow	763 kg/hr
Ammonia flow	535 kg/hr
Host nutrients flow	312 kg/hr
Sulfur dioxide flow	74 kg/hr
Glucose price	$569/ton
Corn steep liquor price	$56/ton
Ammonia price	$440/ton
Host nutrients price	$806/ton
Sulfur dioxide price	$298/ton
Cooling water demand	66913 kW
Cooling water cost	$0.05/ton
Variable operating costs	**$67,101,085/yr**
Fixed operating costs	**$11,953,217/yr**
Total annualized cost	**$93,661,009/yr**
Heat demand	10194 kW
Electricity demand	27220 kW
Activity level	71909 kg/hr
Parameters	
Cost	$0.155/kg
Heat demand	0.142 kWh/kg
Electricity demand	0.379 kWh/kg

S.2.2.3. Fermentation and alcohol 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 ethanol and isobutanol recovery. The NRTL-RK thermodynamic package is used. In the simulations, xylose is represented as glucose, and thus we refer to both glucose and xylose as *sugars*. The process simulation is shown in Figure 5 (Section 5.5).

Note that the fraction of sugars in the hydrolysate that react to produce isobutanol and ethanol are based on the experimental yields (Section 2.1). The bioreactor model considers the fermentation reactions $C_6H_{12}O_6 \rightarrow C_4H_{10}O + 2CO_2 + H_2O$ and $C_6H_{12}O_6 \rightarrow 2C_2H_6O + 2CO_2$, which have theoretical yields of 0.411 kg of isobutanol/kg of sugar and 0.511 kg of ethanol/kg of sugar, respectively. Note that the fermentation reactions that use xylose as substrate have the same theoretical yields of 0.411 kg of isobutanol/kg of xylose and 0.511 kg of ethanol/kg of xylose.

Equipment and installed costs for each unit are determined using the Aspen Process Economic Analyzer (APEA), with the exceptions of the bioreactor and the ethanol dehydration unit. In APEA, construction material SS316 is used for all units. The equipment and installed costs for the bioreactor and the ethanol dehydration unit are estimated based on the prices listed by Humbird et al.[6] The bioreactor cost includes the seed train to inoculate the microorganism in the bioreactor. Note that yeast biomass repitching or selling is not considered. Variable operating costs include the use of cooling water and materials such as corn steep liquor and diammonium phosphate, which are added to the hydrolysate in the bioreactor and seed train. Table S12 shows the economic assumptions to estimate the variable operating costs. Table S13 shows the detailed costs obtained from APEA or literature estimations[6] for the units shown in Figure 5 (Section 5.5). Table S14 summarizes the cost and energy demand of the fermentation and separation processes.

Table S12. Economic assumptions to determine variable operating costs.

Parameter	**Value**
Inoculum medium design basis[a]	10% of hydrolysate
Corn steep liquor (CSL) price	\$56/ton
CSL load in bioreactor	0.25 wt% of hydrolysate
CSL load for the inoculum	0.50 wt% of slurry
Diammonium phosphate (DAP) price	\$970/ton
DAP load in bioreactor	0.33 kg/m^3 hydrolysate
DAP load for the inoculum	0.66 kg/m^3 of slurry
Cooling water price	\$0.05/ton

[a] Slurry diverged from the bioreactor to the inoculum seed train.

Table S13. Detailed cost information of FERM and SEP unit operations.

Unit*	Equip. cost	Installed cost	Var. oper. Cost ($/yr)
Bioreactor[a]	$12,506,689	$20,484,007	$2,256,234
P-101	$17,032	$154,225	
H-101	$78,948	$227,433	
COL-101	$1,257,044	$2,298,794	$403,300
H-102	$83,746	$223,857	$618,040
COL-102	$1,454,272	$2,453,960	$390,440
C-101	$2,430,342	$2,965,378	
H-103	$22,207	$112,823	$141,057
COL-103	$971,083	$1,833,860	$292,659
M-503*	$2,397,478	$4,315,461	$298,130
P-102	$6,587	$52,412	
Decanter	$35,475	$180,572	$43,712
H-201	$11,103	$78,195	
COL-201	$216,423	$758,894	$34,590
H-202	$12,891	$80,359	
COL-202	$220,564	$775,455	$60,478

* Units shown in Figure 5 (Section 5.5)
[a] Estimated from Humbird et al.[6]

Table S14. Summary of costs and energy demand of FERM and SEP blocks.

Item	FERM	SEP
Capital cost		
Equipment cost	$12,506,689	$9,215,194
Installed cost	$20,484,007	$16,511,677
Indirect cost	$15,758,428	$11,611,145
Total capital cost	**$36,242,435**	**$28,122,822**
Operating costs		
Auxiliary materials	$2,072,272/yr	–
Cooling water	$183,962/yr	$2,282,406/yr
Variable operating costs	**$2,256,234/yr**	**$2,282,406/yr**
Fixed operating costs	**$3,280,006/yr**	**$2,561,478/yr**
Total annualized cost	**$9,528,999/yr**	**$7,942,120/yr**
Heat demand	–	83777 kW
Electricity demand	1532.6 kW	665.5 kW
Activity level	38713 kg/hr	9410 kg/hr
Parameters		
Cost	$0.029/kg	$0.100/kg
Heat demand	–	8.903 kWh/kg
Electricity demand	0.040 kWh/kg	0.071 kWh/kg

S.3. Optimization model

In this Section, we present the formal problem statement and the model formulation of the biorefinery.

S.3.1. Problem statement

We are given a set of components $i \in I$ that include the feedstock I^F (*i.e.*, switchgrass), products I^P (*i.e.*, isobutanol and ethanol), 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.2.1). The goal is to minimize the total cost to meet a demand of 1 kg of isobutanol + ethanol.

We introduce the following sets, parameters, and variables (see Figure S2).

Sets

I^S	Solid components (*i.e.*, glucan, xylan, and lignin)
I_j^A	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
$J_j^{IN/OUT}$	Blocks that have streams to/from block j
$J_{i,j}^{IN}$	Blocks that have a stream to block j and component i is present in the stream, *i.e.*, $J_{i,j}^{IN} = \left\{ j' \in J_j^{IN} \mid j \in J, i \in I_{j',j} \right\}$

Parameters

δ	Total demand of alcohols, [kg]
$\eta_{i,j,i'}^{E}$	Conversion of component i to energy i' in block j, [kWh i'/kg i]
π_i^P/π_i^S	Component i purchase/sell price, [\$/kg]
κ	Boiler efficiency
ω^{sugar}	Mass fraction of sugars (*i.e.*, glucose and xylose) in the hydrolysate
ϕ_i	Conversion of mass 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_i^{UT}	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

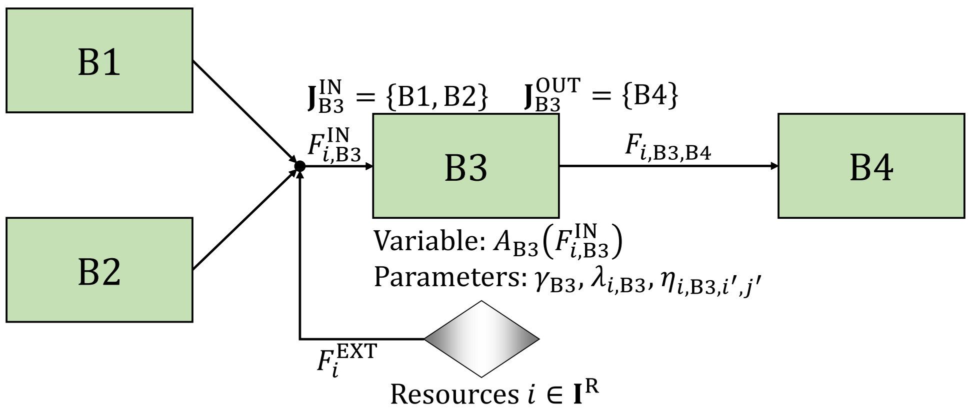

Figure S2. Illustration of a few sets and variables.

S.3.2. Mass balance

The inlet of a block is modeled as a mixer,

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

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,

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

Non-technology blocks, such as the source and the sink are treated differently. Switchgrass ($i = SG$) is converted into its major components (*i.e.*, $I^S = \{glucan, xylan, lignin\}$) when sent to the AFEX block from the source,

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

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

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 alcohols (isobutanol and ethanol),

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

External resources (*i.e.*, natural gas) can be purchased and fed to the combustor block (see Figure S2),

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

S.3.3. 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.3.4.

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.3.4. 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 S15 shows the components used to calculate A_j (*i.e.*, the elements of sets I_j^A).

Table S15. Components used to calculate the activity level of blocks.

Block	I_j^A
FERM	{GLUCOSE, XYLOSE}
SEP	$I^P = \{EtOH, iBuOH\}$
FILT	$I^S = \{GLUCAN, XYLAN, LIGNIN\}$
TBG	$I^E = \{HEAT, ELEC\}$
Others*	$I \backslash I^E$

* 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.3.5. 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.3.6. Minimum fuel selling price

In this work, we determine the minimum fuel selling price (MFSP) on a gasoline gallon equivalent (GGE) basis due to the production of two alcohols. The flows of produced ethanol and isobutanol are converted into GGE flows, and the MFSP is determined by,

$$MFSP = \frac{Cost}{\sum_{i \in I^P} \phi_i F_i^{SNK}} \tag{S16}$$

where $\phi_{iBuOH} = 0.2752$ GGE/kg and $\phi_{EtOH} = 0.2228$ GGE/kg.

S.4. Sensitivity analysis

Sensitivity analysis is carried out using a new set of parameter values in the process optimization model for each studied case. The block parameters are estimated by considering one or multiple improvements following the procedure described in Section S.2.2. The cases considered are (A) a 25% reduction in the switchgrass price, (B) a 50% reduction in the AFEX reactor residence time, (C) a 50% reduction in the NH_3/dry biomass mass ratio during AFEX, (D) a 50% reduction in the enzyme loading during HYD, (E) a 50% increase in the sugar concentration in the hydrolysate, and (F) xylose yields to isobutanol and ethanol of 50% of the experimental glucose yields. Furthermore, three additional cases considered multiple improvements simultaneously. The improved cases are [(B)–(D)], [(A), (E), (F)], and [(A)–(F)]. Table S16 shows the values of the improved parameters for each case studied.

Table S16. Parameter values for each case of the sensitivity analysis.

	Base case	A	B	C	D	E	F	(B)–(D)	(A),(E),(F)	(A)–(F)
Switchgrass price [$/Mg]	101	76	101	101	101	101	101	101	76	76
AFEX residence time [min]	30	30	15	30	30	30	30	15	30	15
NH3/dry biomass load [g/g]	1.0	1.0	1.0	0.5	1.0	1.0	1.0	0.5	1.0	0.5
Enzyme loading [mg/g glucan]	93	93	93	93	46.5	93	93	46.5	93	46.5
Hydrolysate sugar concentration [g/L]	96.3	96.3	96.3	96.3	96.3	144.5	96.3	96.3	144.5	144.5
γ_{AFEX} [$/kg]	0.034	0.034	0.026	0.025	0.034	0.034	0.034	0.019	0.034	0.019
γ_{HYD} [$/kg]	0.155	0.155	0.155	0.155	0.088	0.155	0.155	0.088	0.155	0.088
γ_{FERM} [$/kg]	0.029	0.029	0.029	0.029	0.029	0.020	0.035	0.029	0.020	0.020
γ_{SEP} [$/kg]	0.100	0.100	0.100	0.100	0.100	0.071	0.075	0.100	0.059	0.059
$\lambda_{HEAT,AFEX}$ [kWh/kg]	0.665	0.665	0.665	0.333	0.665	0.665	0.665	0.333	0.665	0.333
$\lambda_{HEAT,HYD}$ [kWh/kg]	0.142	0.142	0.142	0.142	0.126	0.142	0.142	0.126	0.142	0.126
$\lambda_{HEAT,SEP}$ [kWh/kg]	8.903	8.903	8.903	8.903	8.903	5.683	6.890	8.903	4.493	4.493
$\lambda_{ELEC,AFEX}$ [kWh/kg]	0.035	0.035	0.035	0.018	0.035	0.035	0.035	0.018	0.035	0.018
$\lambda_{ELEC,HYD}$ [kWh/kg]	0.379	0.379	0.379	0.379	0.206	0.379	0.379	0.206	0.379	0.206
$\lambda_{ELEC,FERM}$ [kWh/kg]	0.040	0.040	0.040	0.040	0.040	0.026	0.040	0.040	0.026	0.026
$\lambda_{ELEC,SEP}$ [kWh/kg]	0.071	0.071	0.071	0.071	0.071	0.054	0.056	0.071	0.050	0.050
EtOH recovery in SEP [kg/kg]	0.973	0.973	0.973	0.973	0.973	0.983	0.975	0.973	0.990	0.990
iBuOH recovery in SEP [kg/kg]	0.995	0.995	0.995	0.995	0.995	0.999	0.994	0.995	0.999	0.999

S.5. Heat and electricity consumption profiles

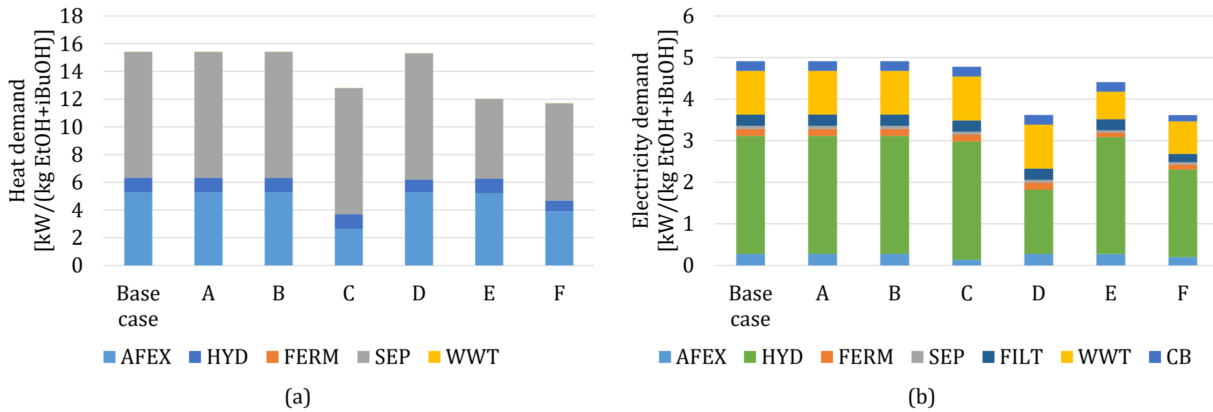

Figure S3. Energy demand in each block of the base case design and sensitivity analysis cases. (a) Heat demand; (b) electricity demand.

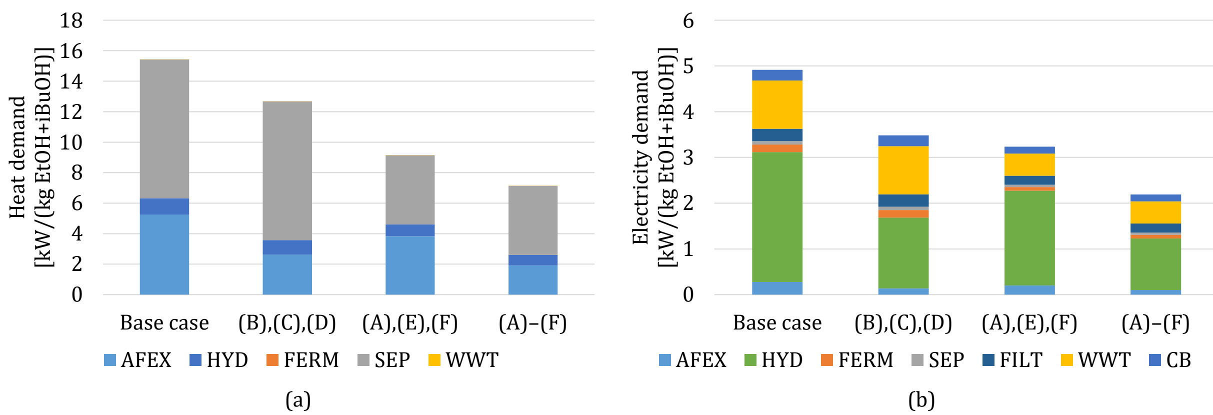

Figure S4. Energy demand in each block of the sensitivity analysis combined cases. (a) Heat demand; (b) electricity demand.

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