System-Level Analysis of Lignin Valorization in Lignocellulosic Biorefineries

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HIGHLIGHTS
- Developed optimization model to evaluate biorefinery with lignin valorization
- Studied impact of technical, economic, and energy parameters on economics
- Lignin utilization is optimized to achieve a thermal-neutral biorefinery
- Established technology targets for economic and energetic feasibility

GVL: γ-valerolactone pretreatment
COFER: Co-fermentation
SEP: Separation
WWT: Wastewater treatment
LV: Lignin valorization
CB: Combustor & boiler
TBG: Turbogenerator

No lignin valorization
With lignin valorization
Valorized lignin: 40%
System-Level Analysis of Lignin Valorization in Lignocellulosic Biorefineries

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SUMMARY

We study the economics and energy efficiency of biorefineries employing lignin valorization. We use superstructure-based process synthesis to study different configurations under different types of constraints. Using optimization, we examine the impact of various parameters for lignin valorization such as bioproduct selling price, production cost, conversion coefficient, and energy requirement. The results show that the optimal strategy leading to a minimum ethanol selling price (MESP) of $3.44/GGE does not include lignin valorization. Results indicate that under certain scenarios, the optimal biorefinery strategies with lignin valorization tend to be energy deficient, and thus the optimal pretreatment technology may switch from γ-valerolactone-based deconstruction to ammonia fiber expansion. Further analysis is performed to study how improvements in combinations of selected parameters can lead to lower cost for a thermal-neural biorefinery.

INTRODUCTION

Fossil-based fuels and chemicals have provided the majority of energy needed for human development over the last century (U.S. Energy Information Administration, 2018). However, with the rising concerns over global warming and depleting fossil resources, the global community has come to the conclusion that a switch to renewable sources is critical to sustain future developments (UNGA, 2015). In US, a potential biomass availability of more than 1 billion dry tons per year is projected by 2030 providing a large resource for renewable energy (Langholtz et al., 2016). Lignocellulosic biomass is of particular interest as it can be collected in large quantities from agricultural and forestry resources and is inedible and carbon neutral, avoiding food vs fuel issues associated with grain and crop based biomass (Sun et al., 2018).

Lignocellulosic biomass has three major constituents: cellulose, hemicellulose, and lignin (Mussatto, 2016). Cellulose (30–50 wt%) is a linear chain polysaccharide consisting of hundreds to thousands of β (1→4)-linked D-glucose molecules (Upton and Kasko, 2016). Hemicellulose (20–35 wt%) is an amorphous heteropolymer of primarily xylose sugars (Gibson, 2012). Lignin (15–30 wt%) is a complex aromatic heteropolymer derived from three cinnamyl alcohol monomers, i.e., p-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol linked by carbon-carbon and ether bonds producing, respectively, p-hydroxyphenyl (H), guaiacyl (G), and syringyl phenylpropanoid (S) units in lignin polymer (Boerjan et al., 2003; Ralph et al., 2019). To develop economical and sustainable biorefineries, all three major constituents must be effectively converted to value-added products. Over the last decades, significant progress has been made in cellulose and hemicellulose deconstruction and monomer upgrading technologies to fuels and chemicals (Chandel et al., 2018; Langan et al., 2011; Op de Beeck et al., 2015; Peng et al., 2012; Zabed et al., 2016). In contrast, lignin valorization technologies have been limited, for the most part, to heat and power production (Da Costa Sousa et al., 2016; Vardon et al., 2015).

Native lignin is covalently cross-linked with hemicellulose, which together form an amorphous structure to enclose and protect cellulose fibers from microbial attack (Schutyser et al., 2018). Biomass deconstruction is performed to breakdown the covalent bonds with holocellulose (cellulose and hemicellulose) and yield isolated lignin prior to valorization. Generally, fractionation strategies can be divided into two categories: (1) methods resulting in lignin release from the biomass called delignification and (2) methods targeting conversion and solubilization of carbohydrates. Delignification processes include alkaline, acidic, reductive, ionic liquid dissolution, and mechanical pretreatment followed by extraction, which produce lignin precipitate or depolymerized lignin oil. The second category includes acid-catalyzed hydrolysis, enzyme-assisted hydrolysis, and thermal processes, which isolate lignin in the form of precipitate or insoluble residue. See Schutyser et al. (Schutyser et al., 2018) for a detailed review of each category.
Native lignin polymer contains carbon-carbon and ether inter-unit connections (Boerjan et al., 2003; Vanholme et al., 2010). The most abundant linkage bond (>50%) is β-O-4 alkyl-aryl ether linkage, which, along with α-O-4 ether linkage, is the most easily cleavable bond (Chakar and Ragauskas, 2004). Considering that carbon-carbon bonds are difficult to break, the majority of lignin depolymerization strategies target the ether bonds (Gall et al., 2017; Rahimi et al., 2014). Generally, the theoretical monomer yield is proportional to the square of the relative content of inter-unit ether bonds (Yan et al., 2008). Therefore, to achieve higher depolymerization yields, the ether bonds must remain intact during biomass fractionation. The monomer yield from lignin strongly depends on three major factors: (1) isolation strategy, (2) depolymerization strategy, and (3) lignin origin (biomass type) (Schutyser et al., 2018). Lignin depolymerization strategies could be categorized to (1) reductive, (2) oxidative, (3) base- and acid-catalyzed, (4) solvolytic and thermal, and (5) two-step depolymerization (Schutyser et al., 2018). Table 1 provides a summary of each category. For a more detailed discussion, readers are referred to reviews of this topic (Behling et al., 2016; Li et al., 2015; Ma et al., 2015; Mu et al., 2013; Schutyser et al., 2018; Xiu and Shahbazi, 2012; Zakzeski et al., 2010).

Some of the lignin depolymerization monomers such as vanillin can be sold without further transformation. However, many other monomer streams require additional processing to narrow the wide range of monomers into targeted categories to (1) favor economical separation and recovery and (2) produce marketable products. Generally, monomer upgrading can be accomplished through biocatalytic or chemocatalytic processes.

In biocatalytic processes, depolymerized lignin is transformed to value-added chemicals mostly using aerobic microbial organisms (Schutyser et al., 2018). Microorganisms could be genetically engineered to defunctionalize aromatic compounds into intermediate products such as gallate, protocatechuate, and catechol. Dioxygenase enzymes could further ring-open the intermediate products and utilize them in central carbon metabolism (Abdelaziz et al., 2016; Masai et al., 2007, 2012). Metabolic engineering has enabled the use of microorganisms for the production of chemicals such as vanillin (Varman et al., 2016), medium-chain-length polyhydroxyalkanoates (Linger et al., 2014), muconic acid (Vardon et al., 2015), pyridine dicarboxylic acids (Mycroft et al., 2015; Perez et al., 2019), and fatty acids (Zhao et al., 2016), which could be further upgraded to high-value chemicals and polymer building blocks.

Chemocatalytic upgrading reactions can be divided into two categories: (1) reactions that transform phenolic core and its substitution degree and (2) reactions that target structure of side-chains (Schutyser et al., 2018). In phenolic core transformation, defunctionalization of core phenol is targeted using hydrodeoxygenation (HDO) reactions to reduce the complexity, functionality, H/C, and O/C ratio in depolymerization products. Accordingly, the HDO reactions could target production of four types of products: (1) alkenes, (2) aromatics, (3) phenols, and (4) cyclohexanols, which are different in oxygen content (depending on partial or complete HDO) and aromaticity (ring hydrogenation or preservation). Table 2 provides a summary of characteristics and operating conditions of monomer upgrading processes. More detailed reviews of upgrading processes are available in the literature (Abdelaziz et al., 2016; Beckham et al., 2016; Bugg and Rahmanpour, 2015; Laskar et al., 2013; Li et al., 2015; Zakzeski et al., 2010).

In summary, lignin is the second most abundant natural polymer accounting for about 30% of organic carbon in the biosphere and is the largest renewable source of aromatic monomers (Li et al., 2018; Stolark, 2017). The polyphenolic structure of lignin can potentially be used to produce value-added chemicals, functional materials, and fuel products (Schutyser et al., 2018; Zhang et al., 2017). However, being at early stage of development, the economic viability of lignin valorization strategies and their integration within biorefineries are not known.

Accordingly, the goal of this paper is to study what technological advances are necessary for lignin valorization technologies to become attractive or, equivalently, what is the impact of uncertainty in some key lignin-valorization-related technological and economic parameters on the viability of lignin valorization strategies. Toward this goal, we first generate a superstructure to represent potential biorefinery configurations (Figure 1) and then a mixed-integer nonlinear programming model (see Methods for details) to identify the optimal process to achieve specific objectives while satisfying given constraints. Using this optimization model, we then evaluate the impact of four critical lignin valorization parameters on the energy efficiency and economics: (1) energy requirement of conversion, (2) conversion efficiency to bioproducts, (3) production cost, and (4) market value of bioproducts.
| Depolymerization | Catalyst | Additives | Solvents | T (°C) | P<sub>O2</sub> (bar) | Selectivity | Yield |
|------------------|----------|-----------|----------|--------|-----------------|-------------|-------|
| Reductive        | Noble metal, base metal, mixed metal | H_2PO_4, HCl, MCI, NaOH, KOH, Na_2CO_3 | H_2O, MeOH, EtOH, iPrOH, dioxane, tetrahydrofuran, or solvent mixture | 130–390 | 10–100 | High toward methoxyphenols or catechols | Moderate <20wt% |
| Mild hydroprocessing (MHD) | Noble metal, base metal | Mostly solventless, MeOH, 1-methylnaphthalene | 320–450 | 35–100 | Low toward phenol, methylated phenols, and phenols with long alkyl chains | Moderate <30wt% |
| Harsh hydroprocessing (HHD) | Noble metal, base metal | H_2O, MeOH, tetrahydrofuran, heptane, methyl cyclohexane, dodecane, hexadecane | 150–320 | 20–70 | High toward cycloalkanes C_2–C_18 | High <50%–70% |
| Bifunctional hydroprocessing (BHD) | Noble metal, base metal | H_2O, formic acid, MeOH, EtOH, iPrOH, tetralin, glycrol | 150–400 | Liquid phase | Very low toward a broad range of compounds | High 20%–86% |
| Liquid phase reforming (LPRD) | H_2O, MeOH, tetrahydrofuran, heptane, methyl cyclohexane, diodecane, hexadecane | | | | | |

| Depolymerization | Catalyst | Additives | Solvents | T (°C) | P<sub>O2</sub> (bar) | Selectivity | Yield |
|------------------|----------|-----------|----------|--------|-----------------|-------------|-------|
| Oxidative        | Soluble catalyst, solid catalyst | O_2 | NaOH in H_2O, MeOH, EtOH, dioxane, tetrahydrofuran, KOH in water | 120–190 | 2–14 | High toward phenolic aldehydes such as vanillin | Low <10%–20% |
| Alkaline oxidation to phenolics (AlOF) | Soluble catalyst, solid catalyst | O_2, H_2O_2, peracetic acid | H_2O, MeOH, acetic acid, methyl isobutyl ketone, ionic liquid | 60–210 | 5–30 | Moderate toward phenols | Low <10%–20% |
| Acidic (AcOF) and pH-neutral (NOF) lignin oxidation to phenolics | Solid catalyst | O_2, H_2O_2 | Mainly liquid phase | 50–225 (liquid phase), 327–377 (gas phase) | High toward carboxylic acids (formic, acetic, succinic, oxalic, and malonic acids) | High 10%–60% |
| Lignin oxidation to non-phenolic carboxylic acids (OCA) | Solid catalyst | O_2, H_2O_2 | Mainly liquid phase | 60–225 (liquid phase), 327–377 (gas phase) | High toward carboxylic acids (formic, acetic, succinic, oxalic, and malonic acids) | High 10%–60% |

| Depolymerization | Catalyst | Additives | Solvents | T (°C) | Selectivity | Yield |
|------------------|----------|-----------|----------|--------|-------------|-------|
| Base- & Acid-Catalyzed | Soluble base (mostly NaOH) or solid base | | H_2O (mostly), MeOH, EtOH, iPrOH, tetrahydrofuran, 3-methyl-3-pentanol | 240–330 | Moderate, methoxyphenols (T < 300), catechol (T > 300) | <10%–20% |
| Base-catalyzed depolymerization (BCD) | Lewis acid, solid or soluble | | H_2O, MeOH, EtOH, iPrOH, 1-BuOH, ethylene glycol, dioxane, octane, formic acid | 140–400 | Low with wide array of products, methoxyphenols (T < 300), catechol (T > 300) | <20%–60% |
| Acid-catalyzed depolymerization (ACD) | Brensted acid | | | | | |

| Depolymerization | Catalyst | Solvents | T (°C) | Selectivity | Yield | Note |
|------------------|----------|----------|--------|-------------|-------|------|
| Solvolytic & Thermal | Water, MeOH, EtOH, iPrOH, 1-BuOH, tetrahydrofuran, acetone, octane, dihydroanthracene, tetralin, naphthalene, solvent mixture | 250–450 | Low | <10%–20% | Hydrogen-donating solvents are mostly used |

Table 1. Summary and Characteristics of Lignin Depolymerization Strategies

(Continued on next page)
Based on our literature review, we determine base values for the parameters describing the lignin depolymerization, monomer upgrading, and bioproduct separation process, defined collectively as the lignin valorization (LV) block. However, to keep the analysis general and given the scarcity of detailed techno-economic analysis (TEA) studies for lignin-based chemical production, we do not specify the target bio-products and conversion and separation technologies used in the LV block. Rather, we establish targets in terms of the four key parameters, thereby providing insights into critical areas of improvement for viable lignin valorization. We do so for strategies considering both depolymerization (Table 1) and monomer upgrading (Table 2).

### RESULTS AND DISCUSSION

#### Base Case

The material and energy balances for the optimal strategy under the base case parameters (see Tables S1–S3 for the base values of the parameters describing each block) are shown in Figure 2. Note that this strategy is the same as the base case strategy ($S_{BC}^{\text{LC}}$) reported by Ng et al. (2019), in which lignin valorization (LV block) is not selected. $S_{BC}^{\text{LC}}$ includes GVL, COFER2, SEP2, WWT, CB, and TBG1 blocks and has a minimum cost of $0.76/\text{kg ethanol}$, which is equivalent to a minimum ethanol selling price (MESP) of $3.44/$GGE. If we enforce the selection of lignin valorization by fixing the binary variable for the LV block ($Y_V = 1$), the lignin stream from the GVL block will be split, and a fraction of it will be sent to LV satisfying the lower bound on production level. Thus, the optimal solution in this case, referred to as $S_{BC-LV}^{\text{SC}}$ (see Figure 2), will depend on the selected lower capacity (e.g., $z_{LV} = 0.039$).

In the reminder of the paper, we study how changes in four key parameters for LV alter the optimal design, economics, and energy efficiency of a lignocellulosic biorefinery. In other words, we study how uncertainty in these parameters impact the optimal biorefinery configuration and its key performance metrics. Before we present the detailed results, we note that a number of other parameters are stochastic. However, although the impact of uncertainty in these parameters on the minimum ethanol cost can be significant (see Figure S4), the major insights of this study, in terms of technological targets, remain the same (see discussion in Transparent Methods). This is because these other parameters impact both the lignin-to-heat/power and lignin-to-bioproducts strategies. For example, an increase in feedstock price will lead to a more expensive lignin stream, but the fundamental trade-off we study (lignin-to-heat/power vs. lignin

| Depolymerization | Catalyst 1st Stage | Catalyst 2nd Stage | T (°C) | Selectivity | Yield | Note |
|-------------------|-------------------|-------------------|-------|-------------|-------|------|
| Fast pyrolysis (FPD) | 4-acetoamide-TEMPO/HNO$_3$/HCl, DDQ/tBuONa, [4-AcNH-TEMPO][BF$_4$]-mediated, NHPI/2,6-lutidine-mediated | Aqueous formic acid/sodium formate | 110 | Phenolic diketones (syringyl-and guaiacyl-1,2-propanedione), aldehydes (syringaldehyde and vanillin), and acids (syringic, vanillic, and p-hydroxybenzoic acid) | 52% | Under aerobic oxidation or electrocatalytic oxidation |
| Catalytic fast pyrolysis (CFP) | Benzylic alcohol oxidation and depolymerization (BAOD) | Benzylic alcohol methylation and depolymerization (BAMD) | 280 | Low | 17% | Under microwave radiation and methanol solvent |

**Table 1. Continued**

Based on our literature review, we determine base values for the parameters describing the lignin depolymerization, monomer upgrading, and bioproduct separation process, defined collectively as the lignin valorization (LV) block. However, to keep the analysis general and given the scarcity of detailed techno-economic analysis (TEA) studies for lignin-based chemical production, we do not specify the target bio-products and conversion and separation technologies used in the LV block. Rather, we establish targets in terms of the four key parameters, thereby providing insights into critical areas of improvement for viable lignin valorization. We do so for strategies considering both depolymerization (Table 1) and monomer upgrading (Table 2).
valorization) will not be noticeably impacted. Thus, although the minimum ethanol cost may change, the trends and the parameter values of the LV block at which strategy transitions occur will remain practically the same.

**Analysis**

To identify the major drivers for lignin valorization, we study the impact of the following parameters on the optimal biorefinery configuration and minimum ethanol cost: (1) conversion coefficient, (2) unit conversion cost, (3) bioproduct selling price, and (4) energy requirement. The first two depend on the efficiency of both conversion and separation technology employed within the valorization block, whereas the third one depends on the selected bioproduct. Additionally, the energy requirement depends on the energy input necessary for conversion (e.g., heat) and separation (e.g., heat and power). We note that, from a sustainability standpoint, a thermal-neutral biorefinery is always favorable, especially for biofuel, as opposed to biochemical, production (Humbird et al., 2011). Here, the term “thermal-neutral” refers to a biorefinery that is energetically self-sufficient through byproduct stream burning (e.g., unconverted lignin, biogas from anaerobic digestion, and biomass sludge from WWT) to generate steam and electricity and additional revenue through excess electricity sale (Humbird et al., 2011).

**Conversion Coefficient and Bioproduct Selling Price**

First, the sensitivity of the minimum ethanol cost is evaluated with respect to conversion coefficient and bioproduct selling price at a fixed unit conversion cost ($0.16/kg-lignin) and energy requirement (2.7 kWh/kg-lignin of heat and 0.05 kWh/kg-lignin of electricity) for the LV block. The results of this analysis are shown in Figure 3A. The minimum ethanol cost decreases with the increase of conversion coefficient and bioproduct selling price if the LV block is selected. In contrast, the minimum ethanol cost remains the same for the S$^{PC}$ strategy at the bottom left region (region on the left of the white dashed line), which is selected when the conversion coefficient and bioproduct selling price are low.

| Upgrading Process | Target Products | Product Value | C-H-O Ratio | Catalyst | Note |
|-------------------|-----------------|---------------|-------------|----------|------|
| Chemocatalytic    | Alkanes and cyclohexanes | Low-value, mid-range fuel additive | High H/C, low O/C | Noble metals (Ru, Rh, Pd, Pt), Ni-based catalyst, H3PO4, acetic acid, acidic IL, HZSM-5, HBEA | Monomers are ring opened and products are fully deoxygenated |
|                   | Aromatic hydrocarbons | Low value, mid-range fuel additive | Low H/C, low O/C | Co-Mo, NiMo, MoO3, FeMoP, Ru/TiO2, PdFe/C, PtCo/C | Operated at gas phase, high temperature, and low H2 pressure (<1 bar) for CO hydrogenation. Products are fully deoxygenated |
|                   | Cyclohexanols    | As feed for synthesis of high-value monomers (e.g., adipic acid and polyester building blocks) | High H/C, high O/C | Ni/CeO2, Ni/SiO2-Al2O3, RANEYs Ni, CoN/C/Ru/ZrO2-La(OH)3, Ru–MnO2/C, and Ru/C + MgO | Operated in liquid phase, partial HDO, demethoxylation, and aromatic ring hydrogenation |
|                   | Phenols         | As feed for synthesis of high-value monomers (e.g., terephthalic acid, ethylene, propylene, and phenol) | Low H/C, high O/C | Noble metal, base metal, Selective demethoxylation |
| Biological        | Vanillin, medium-chain-length polyhydroxyalkanoates, muconic acid | Precursor to adipic acid, terephthalic acid, pyridine dicarboxylic acids, and fatty acids | Close to theoretical yields obtained from representative components such as p-coumarate, ferulate, and benzoate |

Table 2. Summary and Characteristics of Upgrading Strategies for Lignin-Derived Monomers
Figure 3 can also be used to predict the economic feasibility of a lignin valorization technology. For example, if a technology is developed to further convert intermediate bioproducts (e.g., monomers) to a high-value chemical via monomer upgrading (e.g., see strategies listed in Table 2), the selling price of the chemical should be at least $1.3/kg if 80% yield is achieved for this additional step (0.24 overall conversion coefficient).

We also observe that the optimal pretreatment technology switches from GVL to AFEX at the top right region, above the gray dashed line, if both conversion coefficient (>0.43 kg-bioproduct/kg-lignin) and bioproduct selling price (> $2.6/kg) are high. Figure 4 shows the optimal strategies with the GVL block and AFEX block, respectively, based on the same conversion coefficient (0.48 kg-bioproduct/kg-lignin) and bioproduct selling price ($2.8/kg). The optimal strategy with the AFEX block has a higher product yield but also higher energy requirement than the one with the GVL block. To illustrate the trade off, we plot the minimum ethanol cost as a function of bioproduct price with fixed conversion coefficient for the two strategies (see Figure 5). Although the minimum ethanol cost of both strategies decreases with the bioproduct selling price, a higher product yield (0.362 kg-bioproduct/kg-ethanol vs 0.284 kg-bioproduct/kg-ethanol) leads to a faster reduction and it offsets the exceeded production cost when the bioproduct price goes beyond $2.73/kg.

Figure 1. Corn Stover-to-Ethanol Superstructure
Abbreviations—AFEX: ammonia fiber expansion, AHP: copper-catalyzed alkaline hydrogen peroxide, CB: combustor and boiler, COFER: co-fermentation, DA: dilute acid, EA: extractive ammonia, GVL: γ-valerolactone, HYD: hydrolysis, LV: lignin valorization, SEP: separation, SSCF: simultaneous saccharification and co-fermentation, SV: stillage valorization, TBG: turbogenerator, WWT: wastewater treatment.

Figure 2. Strategies $S^{SC}$ (GVL-COFER2-SEP2-WWT-CB-TBG1) and $S^{SC-LV}$ (GVL-COFER2-SEP2-LV-WWT-CB-TBG1)
The faded arcs that are connected to the LV block are only applicable to the $S^{SC-LV}$ strategy. Black fonts before the SEP2 block are identical for both $S^{SC}$ and $S^{SC-LV}$ strategies, whereas blue and red fonts after the SEP2 block represent the flows related to $S^{SC}$ and $S^{SC-LV}$ strategies, respectively.
The optimal strategies with lignin valorization tend to be energetically deficient because the generated energy from the remaining lignin is not sufficient to meet biorefinery demand (see region above and to the right of the white dashed dot line in Figure 3A). When LV is selected, natural gas and/or electricity is purchased because revenue from bioproducts sales is higher than the cost of purchased energy. Thus, we next consider strategies subject to the constraint that neither natural gas nor electricity is purchased. The strategy with the AFEX block is no longer selected (see Figure 3B) because it requires more energy than the one with the GVL block. Unlike the strategies leading to the results in Figure 3A, the optimal strategies with the LV block do not fully valorize lignin. Instead, a fraction of lignin is used for heat and power generation; the split ratio is determined by the conversion coefficient of the LV block. For example, 50% of lignin is used to produce bioproduct if the conversion coefficient is 0.24 and bioproduct selling price is greater than $1.2/kg. When the conversion coefficient increases, the utilization of lignin in the LV block decreases. Overall, when energy-related constraints are added, the optimal strategies with the LV block have higher minimum ethanol cost than those in Figure 3A. Because a thermal-neutral biorefinery is preferred, the following analysis focuses on the strategies with no externally purchased natural gas and/or electricity.

**Production Cost and Bioproduct Selling Price**

Here, for the LV block, we define the production cost ($/kg-bioproduct) as the quotient of the unit conversion cost ($/kg-lignin) by the conversion coefficient (kg-bioproduct/kg-lignin). This allows us to study the minimum ethanol cost as a function of the bioproduct selling price and production cost at a fixed conversion coefficient ($0.3 kg-bioproduct/kg-lignin) by changing its unit conversion cost. Clearly, higher bioproduct selling price and lower production cost lead to lower minimum ethanol cost. Because the conversion coefficient is fixed, the fraction of valorized lignin is 45%, whereas the remaining lignin is sent for heat and power generation. Similar to Figure 3B, the GVL block is preferred for pretreatment along with the LV block when the biorefinery is thermal-neutral.

Alternatively, we can plot the minimum ethanol cost in terms of the bioproduct selling price and production cost, considering a unit conversion cost equal to $0.162/kg-lignin but changing the conversion coefficient (see Figure 6B). Parameter combinations below and to the right of the white dashed line lead to lower minimum ethanol cost than those in Figure 6A. This indicates that conversion coefficient improvements are preferred over unit conversion cost reductions for the same production cost because an increase in bioproduct production leads to more revenue. Also, we see that the lignin utilization ratio is correlated with the conversion coefficient if the LV block is selected. For example, in Figure 6B, 50% lignin utilization...
corresponds to a production cost of $0.675/kg-bioproduct, which is equivalent to 0.24 kg-bioproduct/kg-lignin conversion coefficient when the unit conversion cost is fixed at $0.162/kg-lignin. This is consistent with the correlation between conversion coefficient and lignin utilization in Figure 6B.

Profit and Energy Requirement

To understand the trade-offs between the economic and energy-related drivers, we combine all parameters considered in the previous sections in one parameter (called “profit”) and study its impact, along with the impact of energy requirement (kWh/kg-bioproduct), on the minimum ethanol cost. The profit ($/kg-bioproduct) for the LV block is calculated by

\[
\text{Profit} = \frac{\text{Bioproduct selling price}}{\text{Conversion cost}}
\]

For illustration, we change the profit by varying the bioproduct selling price from $0.5–3.0/kg while keeping the other parameters at their base case values. The results are shown in Figure 7. No lignin valorization is selected when the combination of profit and energy requirement is on the left of the white dashed line. Furthermore, since the conversion coefficient is fixed, the lignin utilization percentage of the LV block is now correlated with its energy requirement. A higher energy requirement leads to a lower ratio of lignin valorized to bioproduct because more lignin would be required to fulfill the energy demand for a thermal-neutral biorefinery.
Conclusion

In this paper, we studied biorefinery strategies for the conversion of biomass to ethanol coupled with lignin valorization subsystems. Based on process synthesis through superstructure optimization, thousands of optimizations were performed to evaluate the impact of various parameters related to lignin valorization on the optimal biorefinery configuration and minimum ethanol cost. Interestingly, we showed that different pretreatment technologies may be selected under different constraints. Our analysis provided baseline results and suggested what advances can make lignin valorization economically attractive. We hope that our results coupled with the identification of appropriate lignin-derived products and development of economical separation technologies for bioproduct recovery will help accelerate the development of lignin valorization technologies.
Limitations of the Study

Our goal is to identify general insights, and thus detailed analysis for specific lignin valorization products or strategies was not performed. However, detailed techno-economic analysis, including an assessment of the impact of uncertainty in key parameters (describing blocks other than LV), would become necessary when specific compounds and a detailed production process, including viable separation and recovery blocks, are identified.

METHODS

All methods can be found in the accompanying Transparent Methods supplemental file.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.100751.

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AUTHOR CONTRIBUTIONS

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DECLARATION OF INTERESTS

The authors declare no competing interests.
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Supplemental Information

System-Level Analysis of Lignin Valorization in Lignocellulosic Biorefineries

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Supplemental Figures

**Figure S1.** Representation of a general superstructure. B1 – B5 are blocks; C1 – C5 are components; SR1 and P1 – P2 are source and products, Related to Figure 1.

**Figure S2.** (A) Example of sets, subsets and binary parameters. (B) – (E) Generic mass and energy flow, Related to Figure 1.
Figure S3. Histograms of values of parameters used for the assessment of the impact of uncertainty on the ethanol cost of the base case strategy. (A) Feedstock price, (B) Electricity export price, (C) Production cost variation, and (D) Lignin conversion coefficient in GVL block. Note that production cost variation is used as a multiplier to the sum of the production costs of all process blocks, Related to Figure 2.
Figure S4. Distribution of the minimum ethanol cost of the base case in the scenarios generated by varying the values of four key parameters not directly related to lignin valorization (histograms of values shown in Figure S3), Related to Figure 2.
## Supplemental Tables

### Table S1. Composition of feedstock and unit price of components, Related to Figure 1.

| Item                        | Value  |
|-----------------------------|--------|
| **Composition of Corn Stover** |        |
| Glucan                      | 0.496  |
| Xylan                       | 0.293  |
| Lignin                      | 0.211  |
| **Unit Price \( \lambda_i \) ($ kg\textsuperscript{-1} or *$ kWh\textsuperscript{-1})** |        |
| Corn Stover                 | 0.100  |
| Natural Gas (purchase)      | 0.600  |
| Electricity (export)        | 0.060* |
| Electricity (purchase)      | 0.065* |
| Bioproducts (SV)            | 2.000  |
| Bioproducts (LV)            | 1.000  |

### Table S2. Conversion coefficient of each block, Related to Figure 1.

| \( i \) | \( i' \) | \( j \) | \( p_n \) | \( p_n' \) | \( \eta_{s,i',p} \) |
|---------|---------|---------|---------|---------|---------|
| Glucan  | Glucose | DA      | I1      | O1      | 0.111   |
| Glucan  | Glucan  | DA      | I1      | O1      | 0.900   |
| Xylan   | Xylose  | DA      | I1      | O1      | 1.023   |
| Xylan   | Xylan   | DA      | I1      | O1      | 0.100   |
| Lignin  | Lignin  | DA      | I1      | O1      | 0.950   |
| Glucan  | Glucose | HYD1    | I1      | O1      | 1.000   |
| Glucan  | Glucan  | HYD1    | I1      | O1      | 0.100   |
| Xylan   | Xylan   | HYD1    | I1      | O1      | 1.000   |
| Glucose | Glucose | HYD1    | I1      | O1      | 0.891   |
| Xylose  | Xylose  | HYD1    | I1      | O1      | 0.871   |
| Lignin  | Lignin  | HYD1    | I1      | O1      | 1.000   |
| Glucose | Ethanol | COFER1  | I1      | O1      | 0.486   |
| Xylose  | Ethanol | COFER1  | I1      | O1      | 0.434   |
| Glucose | Glucose | COFER1  | I1      | O1      | 0.050   |
| Xylose  | Xylose  | COFER1  | I1      | O1      | 0.150   |
| Glucan  | Glucan  | COFER1  | I1      | O1      | 0.990   |
| Xylan   | Xylan   | COFER1  | I1      | O1      | 0.990   |
| Lignin  | Lignin  | COFER1  | I1      | O1      | 1.000   |
| Glucose | Ethanol | SSCF    | I1      | O1      | 0.350   |
| Xylose  | Ethanol | SSCF    | I1      | O1      | 0.330   |
| Glucan  | Ethanol | SSCF    | I1      | O1      | 0.510   |
| Glucan  | Glucose | SSCF    | I1      | O1      | 0.060   |
| Xylose  | Xylose  | SSCF    | I1      | O1      | 0.150   |
**Table S2 (continued). Conversion coefficient of each block, Related to Figure 1.**

| $i$         | $i'$       | $j$       | $p_n$ | $p_n'$ | $\eta_{i, i'}$ |
|-------------|------------|-----------|-------|--------|----------------|
| Glucan      | Glucan     | SSCF      | I1    | 01     | 0.089          |
| Xylan       | Xylan      | SSCF      | I1    | 01     | 0.990          |
| Lignin      | Lignin     | SSCF      | I1    | 01     | 1.000          |
| Ethanol     | Ethanol    | SEP1      | I1    | 01     | 0.950          |
| Glucose     | Glucose    | SEP1      | I1    | 02     | 1.000          |
| Xylose      | Xylose     | SEP1      | I1    | 02     | 1.000          |
| Glucan      | Glucan     | SEP1      | I1    | 03     | 1.000          |
| Xylan       | Xylan      | SEP1      | I1    | 03     | 1.000          |
| Lignin      | Lignin     | SEP1      | I1    | 03     | 1.000          |
| Glucose     | Bioproducts (SV) | SV | I1    | 01     | 0.300          |
| Glucose     | Glucose    | SV        | I1    | 02     | 0.700          |
| Xylose      | Xylose     | SV        | I1    | 02     | 0.700          |
| Glucose     | Biogas     | WWT       | I1    | 01     | 0.267          |
| Xylose      | Biogas     | WWT       | I1    | 01     | 0.733          |
| Biogas      | Heat       | CB        | I1    | 01     | 16.670         |
| Glucan      | Heat       | CB        | I1    | 01     | 7.580          |
| Xylan       | Heat       | CB        | I1    | 01     | 7.580          |
| Lignin      | Heat       | CB        | I1    | 01     | 8.200          |
| Lignin      | Bioproducts (LV) | LV | I1    | 01     | 0.300          |
| Lignin      | Lignin     | LV        | I1    | 02     | 0.700          |
| Glucan      | Glucan     | LV        | I1    | 02     | 1.000          |
| Xylan       | Xylan      | LV        | I1    | 02     | 1.000          |
| Glucan      | Glucan     | AFEX      | I1    | 01     | 0.950          |
| Xylan       | Xylan      | AFEX      | I1    | 01     | 0.950          |
| Lignin      | Lignin     | AFEX      | I1    | 01     | 0.950          |
| Glucan      | Glucose    | HYD2      | I1    | 01     | 0.800          |
| Glucan      | Glucan     | HYD2      | I1    | 01     | 0.100          |
| Xylan       | Xylan      | HYD2      | I1    | 01     | 0.100          |
| Xylan       | Xylose     | HYD2      | I1    | 01     | 0.795          |
| Lignin      | Lignin     | HYD2      | I1    | 01     | 1.000          |
| Heat        | Electricity | TBG    | I1    | 01     | 0.750          |
| Natural Gas | Heat       | CB        | I1    | 01     | 13.880         |
| Lignin      | Lignin     | AHP       | I1    | 01     | 0.784          |
| Glucan      | Glucan     | AHP       | I1    | 02     | 0.950          |
| Xylan       | Xylan      | AHP       | I1    | 02     | 0.548          |
| Glucan      | DGlucan    | AHP       | I1    | 02     | 0.050          |
| Xylan       | DXylan     | AHP       | I1    | 02     | 0.453          |
| Lignin      | Lignin     | AHP       | I1    | 02     | 0.216          |
**Table S2 (continued). Conversion coefficient of each block, Related to Figure 1.**

| $i$          | $i'$        | $j$          | $p_n$ | $p_{n'}$ | $\eta_{i_p,i_p'}$ |
|-------------|-------------|--------------|-------|----------|-------------------|
| Glucan      | Glucose     | HYD3         | I1    | 01       | 1.089             |
| Xylan       | Xylose      | HYD3         | I1    | 01       | 1.057             |
| DGlucan     | Glucose     | HYD3         | I1    | 01       | 1.111             |
| DXylan      | Xylose      | HYD3         | I1    | 01       | 1.136             |
| Lignin      | Lignin      | HYD3         | I1    | 01       | 1.000             |
| Glucan      | Glucan      | HYD3         | I1    | 01       | 0.010             |
| Xylan       | Xylan       | HYD3         | I1    | 01       | 0.050             |
| Lignin      | Lignin      | EA           | I1    | 01       | 0.440             |
| Glucan      | Glucan      | EA           | I1    | 02       | 0.960             |
| Xylan       | Xylan       | EA           | I1    | 02       | 0.960             |
| Glucan      | DGlucan     | EA           | I1    | 02       | 0.040             |
| Xylan       | DXylan      | EA           | I1    | 02       | 0.040             |
| Lignin      | Lignin      | EA           | I1    | 02       | 0.560             |
| Glucan      | Glucose     | HYD4         | I1    | 01       | 1.044             |
| Xylan       | Xylose      | HYD4         | I1    | 01       | 0.966             |
| DGlucan     | Glucose     | HYD4         | I1    | 01       | 1.111             |
| DXylan      | Xylose      | HYD4         | I1    | 01       | 1.136             |
| Lignin      | Lignin      | HYD4         | I1    | 01       | 1.000             |
| Glucan      | Glucan      | HYD4         | I1    | 01       | 0.060             |
| Xylan       | Xylan       | HYD4         | I1    | 01       | 0.150             |
| Lignin      | Lignin      | GVL          | I1    | 01       | 0.830             |
| Glucan      | Glucan      | GVL          | I1    | 01       | 0.120             |
| Xylan       | Xylan       | GVL          | I1    | 01       | 0.170             |
| Glucan      | Glucose     | GVL          | I1    | 02       | 0.800             |
| Xylan       | Xylose      | GVL          | I1    | 02       | 0.750             |
| Glucose     | Glucose     | COFER2       | I1    | 01       | 0.130             |
| Xylose      | Xylose      | COFER2       | I1    | 01       | 0.130             |
| Glucose     | Ethanol     | COFER2       | I1    | 01       | 0.485             |
| Xylose      | Ethanol     | COFER2       | I1    | 01       | 0.485             |
| Glucose     | Glucose     | SEP2         | I1    | 02       | 1.000             |
| Xylose      | Xylose      | SEP2         | I1    | 02       | 1.000             |
| Ethanol     | Ethanol     | SEP2         | I1    | 01       | 0.990             |
Table S3. Unit heat and electricity requirement, and unit production cost of different blocks, Related to Figure 1.

| Block  | Heat $\mu_{i=\text{heat}}$ (kWh kg$^{-1}$) | Electricity $\mu_{i=\text{electricity}}$ (kWh kg$^{-1}$) | Production Cost $\theta_j$ ($\$ \text{kg}^{-1}$ or *$\$ \text{kWh}^{-1}$) | Reference                  |
|--------|-------------------------------------------|--------------------------------------------------------|---------------------------------------------------|---------------------------|
| DA     | 0.737                                     | 0.086                                                  | 0.050                                             | Humbird et al., 2011      |
| AFEX   | 0.664                                     | 0.090                                                  | 0.030                                             | Kazi et al., 2010         |
| HYD1   | 0.008                                     | 0.080                                                  | 0.044                                             | Humbird et al., 2011      |
| HYD2   | 0.020                                     | 0.120                                                  | 0.044                                             | Kazi et al., 2010         |
| SSCF   | 0.008                                     | 0.142                                                  | 0.028                                             | Aden et al., 2002         |
| COFER1 | -                                         | 0.045                                                  | 0.060                                             | Humbird et al., 2011      |
| SEP1   | 1.050                                     | 0.054                                                  | 0.025                                             | Humbird et al., 2011      |
| WWT    | 0.004                                     | 1.830                                                  | 0.400                                             | Humbird et al., 2011      |
| LV     | 2.700                                     | 0.050                                                  | 0.162                                             | Ng et al., 2019           |
| CB     | -                                         | 0.058                                                  | 0.060                                             | Humbird et al., 2011      |
| TBG    | -                                         | -                                                      | 0.008*                                            | Humbird et al., 2011      |
| EA     | 2.447                                     | 0.138                                                  | 0.040                                             | Da Costa Sousa et al., 2016|
| AHP    | 0.250                                     | 0.040                                                  | 0.219                                             | Bhalla et al., 2018       |
| HYD3   | 0.008                                     | 0.091                                                  | 0.046                                             | Bhalla et al., 2018       |
| HYD4   | 0.008                                     | 0.091                                                  | 0.046                                             | Bhalla et al., 2018       |
| SEP2   | 0.500                                     | 0.030                                                  | 0.020                                             | Won et al., 2017          |
| COFER2 | 0.555                                     | 0.030                                                  | 0.045                                             | Won et al., 2017          |
| GVL    | 1.000                                     | 0.080                                                  | 0.051                                             | Won et al., 2017          |
| SV     | 5.000                                     | 0.060                                                  | 0.600                                             | Ng et al., 2019           |
**Transparent Methods**

**Optimization-based Process Synthesis**

Optimization-based synthesis involves three major steps: (1) constructing a superstructure with possible process alternatives, (2) formulating an optimization model representing mass and energy balances of the underlying systems, and (3) solving the resulting model to determine the optimal configuration and processing conditions (Wu et al., 2016). Consider a generic superstructure (see Figure S1) consisting of four major elements:

1. **Block**: has one or more operations/technologies (e.g., fermentation, hydrolysis, separation, etc).
2. **Port**: corresponds to stream inlet/outlet point of each block. An inlet port merges substreams from different outlet ports into a parent stream for entering a block, while an outlet port splits the parent stream leaving a block into substreams that flow to different inlet ports (Wu et al., 2016). In particular, a block can have multiple outlet ports, but only one inlet port.
3. **Stream**: connects an outlet and inlet port.
4. **Component**: consists of all chemical components to be included in the studied process. The component flow is carried by each stream.

In this work, each block has a set of technical (conversion coefficient), economic (unit conversion cost), and energy (heat and electricity requirement) parameters, which are obtained from the literature or using simple process models (see the details in the next section “Parameter Determination”). Note that the unit conversion cost has capital, fixed and variable operating cost components. Lower and upper capacity bounds are also defined. For sources and sinks, we obtain the components’ unit prices, as well as their minimum and maximum supplies or demands.

**Parameter Determination**

We first assume the market price of feedstocks, resources, products, and by-products can be found from literature (Bhalla et al., 2018; da Costa Sousa et al., 2016; Humbird et al., 2011; Kazi et al., 2010; Ng et al., 2019; US Environmental Protection Agency, 2018; Won et al., 2017) (Table S1). All costs are indexed to 2017 US dollars and calculated based on a dry mass basis.

Next, we calculate conversion coefficients based on the components exist in the inlet and outlet flows of the block (Table S2). Note that auxiliary inputs (e.g., water, catalyst, enzymes, etc.) do not appear as components in the superstructure, thus they are not included in the calculation of conversion coefficients (see (Kim et al., 2013) for more details). The unit energy consumption of each block (Table S2) is calculated based on the total annual energy divided by the annual consumption rate (exclude auxiliary inputs) of the block. The boiler efficiency is assumed as 80%.

We also calculate the unit production cost (Table S3), which has capital, fixed and variable operating cost components. The capital cost includes the costs of equipment and other miscellaneous costs, e.g., piping and instrumentation, etc. (Humbird et al., 2011). The annualized capital cost is then calculated from the capital multiplied by the capital recovery factor based on 10% of interest rates and 25 years.
of plant’s lifetime. The fixed operating cost includes labor charges, maintenance, etc., while the variable operating cost covers material purchase, waste handling, etc. Auxiliary inputs (e.g., water, catalyst, enzymes, etc.) are included in the calculation of operating costs. The unit production cost is calculated based on the summation of annual operating costs and annualized capital cost, divided by the annual consumption rate of the block (see (Kim et al., 2013) for more details).

**Problem Statement**

We consider a problem with given biomass feedstock (e.g., corn stover, switch grass or pinewood), intermediates (glucose, xylose, and lignin), products (e.g., ethanol, bioproducts, and electricity), as well as external resources (e.g., natural gas and electricity) which are available to purchase if needed. The unit prices of biomass feedstock, products, by-products, and external resources are known. A set of blocks (pretreatment, hydrolysis, fermentation, separation, heat and power generation, etc.) are defined to convert biomass feedstock into ethanol, by-products, and energy. Each block has known energy requirement, conversion efficient, and unit conversion cost. In addition, the lower and upper bounds for (1) capacity of the block, (2) biomass feedstock availability and external resource supplies, and (3) product and by-product demands are also predetermined. We aim to identify the least cost strategy to produce one kg of ethanol. The optimization model has decision variables, such as the material and energy flow of each block, the feedstock and external resources purchase, and the by-product sales.

**Biorefinery Superstructure**

**Figure 1** shows the superstructure for the conversion of corn stover to ethanol (Ng et al., 2019). The corn stover feedstock, consisting of glucan, xylan, and lignin, can be sent to five candidate pretreatment blocks (e.g., dilute acid-based (DA), ammonia fiber expansion-based (AFEX), copper-catalyzed alkaline hydrogen peroxide-based (AHP) (Bhalla et al., 2018), extractive ammonia-based (EA), and γ-valerolactone-based (GVL)). The effluent of the pretreatment block is fed to corresponding hydrolysis and fermentation blocks (e.g., simultaneous saccharification and co-fermentation (SSCF), co-fermentation (COFER1)), to produce sugars (e.g., glucose and xylose) from glucan and xylan. The produced sugars are converted to ethanol. Ethanol is then recovered from water, stillage (glucose and xylose), and solid residues in the separation block (SEP1).

Stillage can be utilized either in the valorization block (SV) to produce and recover value-added bioproducts or in the wastewater treatment block (WWT) to produce biogas. Similarly, solid residues (mainly lignin) can be valorized (LV) to produce value-added bioproducts and/or combusted with biogas from SV in the combustor and boiler (CB) to generate heat. Excessive heat is used to generate electricity in the turbogenerator (TBG). External resources (e.g., natural gas, electricity, etc.) can be purchased if the generated heat and power are not sufficient (i.e., the biorefinery is “energy-deficient”) to satisfy the energy requirement in the biorefinery. Note that both SV and LV blocks have considered the units required for the separation and recovery of high purity bioproducts.
The GVL block includes both conversion and separation; and has two outlet streams: sugars and solid residues. The former is sent to co-fermentation (COFER2) and the subsequent separation (SEP2) directly, while the latter is sent for lignin valorization (LV) and/or heat generation (CB).

All parameter data are provided in the Supplementary Material. All costs are indexed to 2017 US dollars and calculated based on a dry mass basis. The objective function is to minimize the total cost to produce 1 kg of ethanol, which includes the feedstock and additional resource purchases, and the production costs, minus the sales of by-products. Thus, the minimum ethanol cost is equivalent to the minimum ethanol selling price (MESP, the breakeven selling price that leads to zero net present value). The mixed-integer linear programming (MINLP) model is subject to material and energy balance, and constraints that are presented in Supplemental Material. We use GAMS 25.1 with BARON as the global MINLP solver.

**Mathematical Formulation**

Formally, the problem is stated in terms of the following sets and subsets:

a) Components \( i \in I \).
   - \( I^F \): biomass feedstocks; \( I^R \): resources; \( I^I \): intermediates; \( I^E \): energy; \( I^P \): products; \( I^B \): by-products.

b) Blocks \( j \in J \).
   - \( J^{PRE} \): pretreatment; \( J^{HYD} \): hydrolysis; \( J^{FER} \): fermentation; \( J^{SEP} \): separation; \( J^{SV} \): stillage valorization; \( J^{LV} \): lignin valorization; \( J^{WWT} \): wastewater treatment; \( J^{CB} \): combustor and boiler; \( J^{TBG} \): turbogenerator.

c) Port numbers \( pn \in PN \).
   - \( PN^{IN} \): inlet port number; \( PN^{OUT} \): outlet port number.

d) Ports \( p \in P \subset J \times PN \), which is indexed by block and port number.
   - \( P^{IN} \): inlet ports; \( P^{OUT} \): outlet ports; \( P^j^{IN} \): inlet ports of block \( j \); \( P^j^{OUT} \): outlet ports of block \( j \).

e) Streams \( s \in S \subset P \times P \), which is indexed by two ports.
   - \( S_{p'}^{p} \): streams originating from outlet port \( p' \); \( S_j \): streams that are connected to block \( j \).

The binary parameters \( \chi_{i,p',p} \) can be predefined for the component \( i \) present in the stream from outlet port \( p' \) and inlet port \( p \) after the superstructure is generated. The examples of sets, subsets and binary parameters are shown in **Figure S2A**. For example, the stream between outlet port P3 and inlet port P5 does not contain component Cc, therefore \( \chi_{Cc,P3,P5} = 0 \).

The parameters are given as follows:

- \( \lambda_i \): unit price of components \( i \in I^F \cup I^R \cup I^P \cup I^B \) (\$/kg or \$/kWh).
- \( \underline{\theta}_i \leq \overline{\theta}_i \): minimum/maximum supply of components \( i \in I^F \cup I^R \) (kg or kWh).
- \( \underline{\rho}_j \leq \overline{\rho}_j \): minimum/maximum demand of components \( i \in I^P \cup I^B \) (kg or kWh).
- \( \underline{\zeta}_j \leq \overline{\zeta}_j \): lower/upper capacity bounds of block \( j \) (kg or kWh).
\[ \mu_i \]: unit energy \( i \in I^E \) (heat and electricity) requirement of block \( j \) (kWh kg\(^{-1}\)).

\[ \eta_{i,p,i',p'} \]: conversion coefficient (kg kg\(^{-1}\) or kWh kg\(^{-1}\) or kWh kWh\(^{-1}\)).

\[ \theta_j \]: unit production cost of block \( j \) ($ kg\(^{-1}\) or $ kWh\(^{-1}\)).

\[ \kappa \]: boiler efficiency.

Variable \( Y_j \in \{0,1\} \), which is equal to 1 if block \( j \) is selected, and the following nonnegative continuous variables are introduced:

- \( E_{i,p',p}^C \): energy flow between outlet port \( p' \) and inlet port \( p \) (kWh).
- \( E_{i,p}^IN/E_{i,p}^OUT \): inlet/outlet energy flow (kWh).
- \( E_{i}^{SR}/E_{i}^{SK} \): energy flow from/towards source/sink (kWh).
- \( E_{i}^{UT}/E_{i}^{W} \): total energy requirement of biorefinery/waste heat (kWh).
- \( F_{i,p',p}^C \): mass flow between outlet port \( p' \) and inlet port \( p \) (kg).
- \( F_{i,p}^IN/F_{i,p}^OUT \): inlet/outlet mass flow (kg).
- \( F_{i}^{SR}/F_{i}^{SK} \): mass flow from/towards source/sink (kg).
- \( R_{i,p',p} \): split fraction of stream between outlet port \( p' \) and inlet port \( p \).
- \( X_j \): total consumption level of block \( j \) (kg).
- \( Z \): total cost ($).

**Material Balance**

The feedstock flow is converted into flows of the major constituent of biomass (e.g., glucan, xylan, and lignin) through a dummy conversion block (Figure S2B) modeled as follows:

\[
\sum_{i \in I^F} \eta_{i,p''=DFI,i',p'=DFO} F_{i,p}^SR = \sum_{j \in \text{PRE}, p \in P_j^{IN}} \sum_{i \in I^I} F_{i,p}^C \quad \forall i' \in I^I \quad (1)
\]

where \( \eta_{i,p''=i',p'} \) in this equation corresponds to the composition of biomass feedstock. DFI and DFO are dummy inlet port and outlet port, respectively (see Figure S2B).

The inlet mass flow \( F_{i,p}^IN \) (Figure S2C) is given as:

\[
F_{i,p}^IN = \sum_{p' \in P_j^{OUT}} |X_{i,p',p}=1 F_{i,p',p}^C \quad \forall i \in I^I, j \in J^\text{TBG}, p \in P_j^{IN} \quad (2)
\]

where \( F_{i,p',p}^C \) is the connecting flow between outlet and inlet ports.

The outlet mass flow \( F_{i',p}^{OUT} \) is given as:

\[
F_{i',p}^{OUT} = \sum_{i \in I^I, p \in P_j^{IN}} \eta_{i,p,i',p'} F_{i,p}^IN \quad \forall i', j \in J \setminus (J^\text{CB} \cup J^\text{TBG}), p' \in P_j^{OUT} \quad (3)
\]

where \( \eta_{i,p,i',p'} \) is a conversion coefficient.

The outlet mass flow is split at the outlet port:

\[
F_{i,p}^{OUT} = \sum_{p \in P_j^{OUT}} |X_{i,p',p}=1 F_{i,p',p}^C \quad \forall i \in I^I, j \in \left( J^\text{CB} \cup J^\text{TBG} \right), p' \in P_j^{OUT} \quad (4)
\]
The split fraction $R_{p',p}$ is introduced to denote the fraction of stream leaving outlet port $p'$ and entering inlet port $p$ to ensure that the component concentrations in all outgoing streams are the same:

$$P_{i,p'}^{OUT} R_{p',p} = P_{i,p}^{C} \quad \forall i \in I^I, p', p | \chi_{i,p',p} = 1$$

(5)

$R_{p,p'}$ is constrained by the following equations:

$$0 \leq R_{p',p} \leq Y_j \quad \forall j, (p', p) \in S_j$$

(6)

$$\sum_{p' \in S_p} R_{p',p} = Y_j \quad \forall j, p' \in P_{j}^{OUT}$$

(7)

where $Y_j$ is the binary variable for the selection of block $j$.

The mass inflow towards sink (e.g., product and by-product) $F_{i}^{SK}$ is given as:

$$F_{i}^{SK} = \sum_{i \in I^I} \sum_{p \in P^{IN}_{j}} F_{i,p}^{C} \quad \forall i \in I^P \cup I^B$$

(8)

where DPBI is the dummy inlet port of a dummy conversion block (see Figure S2D).

Additional resources (e.g., natural gas) can also be fed to the CB blocks (see Figure S2E):

$$F_{i}^{SR} = \sum_{j \in J^CB} \sum_{p \in P^{IN}} F_{i,p}^{IN} \quad \forall i \in I^R$$

(9)

Energy Balance

The heat generated from the CB blocks $E_{i'}^{heat,p'}$ is given as:

$$E_{i'}^{heat,p'} = \sum_{i \in I^I \cup I^R} \sum_{p \in P^{IN}_{j}} E_{i,p}^{C} \eta_{i,p,i'}^{heat,p'} F_{i,p}^{IN} \quad \forall j \in J^CB, p', p \in P_{j}^{OUT}$$

(10)

After considering boiler efficiency $\kappa$, the heat balance is:

$$\kappa E_{i}^{OUT} = E_{i}^{UT} + E_{i}^{W} + \sum_{p \in P^{IN}_{j}} E_{i,p}^{C} \quad \forall j \in J^CB, p' \in P_{j}^{OUT}$$

(11)

where $E_{i}^{UT}$ is the total energy (heat/electricity) requirement at the biorefinery; $E_{i}^{W}$ is waste heat if no turbogenerator is selected; $E_{i,p'}^{C}$ is the connecting energy flow between two ports. $E_{i}^{UT}$ is determined in the following equation:

$$E_{i}^{UT} = \sum_{j} \mu_{i,j} X_j \quad \forall i \in I^E$$

(12)

where $\mu_{i,j}$ is the unit energy requirement of each block $j$ and $X_j$ is the total consumption level of block $j$, which is given as:

$$X_j = \sum_{i \in I^E \setminus I^I} \sum_{p \in P^{IN}_{j}} F_{i,p}^{IN} \quad \forall j \in J \setminus J^{TBG}$$

(13)

$$X_j = \sum_{i \in I^E} \sum_{p \in P^{IN}} E_{i,p}^{IN} \quad \forall j \in J^{TBG}$$

(14)

The heat inlet flow at the TBG blocks $E_{i,p}^{IN}$ (Figure S2E) is given as:

$$E_{i,\chi_{i,=heat,p'}}^{IN} = \sum_{p' \in P^{OUT}_{j}} \chi_{i,=heat,p',p'} = 1 E_{i,\chi_{i,=heat,p',p'}^{C}} \quad \forall j \in J^{TBG}, p \in P_{j}^{IN}$$

(15)

The electricity generated by the TBG block $E_{i,\chi_{i,=electricity,p'}}^{OUT}$ is given as:
\[ E_i^{\text{OUT;electricity},p'} = \sum_{p \in \mathbf{P}_j} \eta_i = \text{heat,} p, i' = \text{electricity,} p' E_i^{\text{IN;heat}, p} \quad \forall j \in \mathbf{J}_\text{BG}, p' \in \mathbf{P}_j^{\text{OUT}} \] (16)

The electricity balance is given as:
\[ \sum_{j \in \mathbf{J}_\text{BG}} \sum_{p' \in \mathbf{P}_j^{\text{OUT}}} E_i^{\text{OUT;electricity},p'} + E_i^{\text{electricity}} = E_i^{\text{OUT;electricity}} + E_i^{\text{SK;electricity}} \] (17)

where electricity \( E_i^{\text{SR}} \) and \( E_i^{\text{SK}} \) can be purchased and sold from and to the market, respectively.

**Bounds**

The product and by-product are bounded as follows:
\[ \rho_i \leq F_i^{\text{SK}} \leq \bar{\rho}_i \quad \forall i \in \mathbf{I}_P \cup \mathbf{I}_B \setminus \mathbf{I}_E \] (18)
\[ \rho_i \leq E_i^{\text{SK}} \leq \bar{\rho}_i \quad \forall i \in \mathbf{I}_B \cap \mathbf{I}_E \] (19)

Similarly, the feedstock and resource flows are bounded as follows:
\[ \vartheta_i \leq F_i^{\text{SR}} \leq \bar{\vartheta}_i \quad \forall i \in \mathbf{I}_F \cup \mathbf{I}_R \setminus \mathbf{I}_E \] (20)
\[ \vartheta_i \leq E_i^{\text{SR}} \leq \bar{\vartheta}_i \quad \forall i \in \mathbf{I}_R \cap \mathbf{I}_E \] (21)

The consumption level is bounded by:
\[ \zeta_j Y_j \leq X_j \leq \bar{\zeta}_j Y_j \quad \forall j \] (22)

The following constraints enforce the number of blocks to be selected:
\[ \sum_{j \in \mathbf{J}_\text{PRE}} Y_j = 1, \sum_{j \in \mathbf{J}_\text{HYD}} Y_j = 1, \sum_{j \in \mathbf{J}_\text{FER}} Y_j = 1, \sum_{j \in \mathbf{J}_\text{SEP}} Y_j = 1, \sum_{j \in \mathbf{J}_\text{WWT}} Y_j = 1, \sum_{j \in \mathbf{J}_\text{CB}} Y_j = 1 \] (23)

**Objective Function**

The objective is to minimize the total cost, which includes the feedstock and additional resource purchases, and the total production cost of the biorefinery, minus the sales of by-products.
\[ \text{Min } Z = \left( \sum_{i \in \mathbf{I}_P \setminus \mathbf{I}_E} \lambda_i F_i^{\text{SR}} + \sum_{i \in \mathbf{I}_R \cap \mathbf{I}_E} \lambda_i E_i^{\text{SR}} \right) + \sum_j \theta_j X_j - \left( \sum_{i \in \mathbf{I}_B \setminus \mathbf{I}_E} \lambda_i F_i^{\text{SK}} + \sum_{i \in \mathbf{I}_R \cap \mathbf{I}_E} \lambda_i E_i^{\text{SK}} \right) \] (24)

where \( \lambda_i \) is the unit price of components \( i \) and \( \theta_j \) is the unit production cost of blocks \( j \).

Note that the formulations are linear, except the bilinearities in Equation 5. The MINLP model is implemented in GAMS and solved using BARON.

**Impact of Uncertainty: Major Parameters Not Describing Lignin Valorization**

We study the impact of uncertainty in four parameters (feedstock price, electricity price, production cost, and lignin conversion coefficient in pretreatment) on the ethanol production cost in the base case design (SBC). Specifically, we calculate the cost for 5,000 randomly generated scenarios, where, in each scenario, a value for each one of these four parameters is sampled from the corresponding (triangular) distribution. The assumptions for these distributions are taken from: (A) Feedstock price (Huang et al., 2018), (B) electricity export price (2002-2018 United States industrial average retail price of electricity from U.S. Energy Information Administration), (C) Production cost variation (Merrow et al., 1981), and (D) Lignin conversion coefficient in GVL block (Won et al., 2017). The
parameters of the distributions as well as the histograms of the values used in our evaluation are shown in Figure S3. The optimization model is run for each one of the scenarios, and the distribution of the resulting minimum ethanol cost is shown in Figure S4.

The distribution in Figure S4 suggests that the impact of uncertainty in these parameters on the minimum ethanol cost is substantial. However, this does not mean that the insights, based on the strategy transitions shown in the heat maps in the paper, will change. This is because, as explained in the main text, changes in the four parameters studied here impact both the lignin-to-heat/power and lignin-to-bioproducts strategies.

To illustrate, consider uncertainty in pretreatment (which is one of the most challenging and expensive processing steps for lignocellulosic biomass). An increase in the pretreatment cost will not necessarily change the transition of configurations shown in our figures because more expensive pretreatment means a more expensive lignin stream, regardless of where this lignin stream goes (boiler vs. valorization). It will change the minimum cost of ethanol, that is, the scale of the shown heat maps, but it will not significantly change the actual selection of the lignin valorization block, which is what we aim to study primarily. More generally, uncertainty in the processing parameters (cost, conversion, energy requirement) of almost all blocks, other than lignin valorization, is expected to have, similarly, low impact. There are two exceptions: parameters describing the conversion of lignin to (1) heat and power, and (2) valuable chemicals.

The presented analysis can be viewed as a study of a basic trade-off: benefit from using lignin to produce heat and power (current configuration) versus benefit from valorizing lignin. Thus, it is the uncertainty in blocks CB, TBG, LV (see Figure 1) that will indeed change the results. However, combustion and electricity generation from steam are well known processes and the parameters we use have little uncertainty. Thus, it the uncertainty in lignin valorization, which is at early stages of development and hence subject to significant uncertainty, that is likely to change the selection of the optimal biorefinery strategy and economics. The analysis of the paper can be viewed, precisely, as a study of the impact of uncertainty in some key LV parameters. The heat maps show how the cost and biorefinery configurations change as the values of these uncertain parameters change.
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