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Cellulosic ethanol: status and innovation

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Although the purchase price of cellulosic feedstocks is competitive with petroleum on an energy basis, the cost of lignocellulose conversion to ethanol using today's technology is high. Cost reductions can be pursued via either in-paradigm or new-paradigm innovation. As an example of new-paradigm innovation, consolidated bioprocessing using thermophilic bacteria combined with milling during fermentation (cotreatment) is analyzed. Acknowledging the nascent state of this approach, our analysis indicates potential for radically improved cost competitiveness and feasibility at smaller scale compared to current technology, arising from (a) R&D-driven advances (consolidated bioprocessing with cotreatment in lieu of thermochemical pretreatment and added fungal cellulase), and (b) configurational changes (fuel pellet coproduction instead of electricity, gas boiler(s) in lieu of a solid fuel boiler).

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Introduction

Biofuels are the most established and arguably most promising option available for decarbonizing aviation, ocean shipping, and a substantial fraction of long-haul trucking, without which the 2°C target agreed to at the COP21 meeting is probably not possible to meet [1*]. Lignocellulosic feedstocks are likely required in order to produce biofuels at the level anticipated as part of low

carbon energy scenarios. Consider that whereas 3.1 EJ/year of ethanol are produced from sugar cane and grains today [2*], anticipated global demand for transport modes difficult to decarbonize without biofuels are projected to be at least 50 EJ [1*]. Significant technology export opportunities are likely to arise in response to the world's demand for low-carbon fuels. Cellulosic biofuels also can make important contributions to rural economic development and enhanced sustainability of agricultural landscapes in both developed and developing economies [3,4,5*]. Finally, biomass-derived fuel molecules can be used in conjunction with engine innovations to maximize efficiency and performance [6,7*].

Notwithstanding these motivations, contextual factors impacting cellulosic biofuels have changed substantially in recent years and in general have become more challenging. Widespread deployment of emergent oil extraction technologies such as hydraulic fracturing, horizontal drilling, and tar sands refining have led to an oversupply of oil, lower prices, and decreased energy security concerns for many countries [8]. Exhaustion of global oil resources is a weaker driver for development and deployment of alternative fuels than was the case 5 years ago, and economic barriers to biofuels gaining market share are larger today than they were in the recent past. During this time, we have also seen wide swings in expectations and activity related to cellulosic biofuels, and growth in productive capacity far below that envisioned, —for example, in the Renewable Fuel Standard. Recently-deployed facilities producing cellulosic ethanol at scales approaching commercial, referred to herein as 'pioneer' facilities, represent an important and needed step forward but also bring into focus needs and opportunities for further innovation.

These developments invite a reassessment of needs and opportunities related to development of biologically-based processes for production of cellulosic biofuels, which we endeavor to provide here. We focus on cellulosic ethanol because it is the cellulosic biofuel deployed on the largest scale and is the logical proving ground for new technologies aimed at overcoming the biomass recalcitrance barrier and product diversification.

Status

The equivalent purchase price of biomass on a per barrel oil basis is a function of the purchase price of biomass and

the energy contents of biomass and oil in appropriate units, and may be calculated via Equation (1):

$$Eq P_{\text{Barrel}}^{\text{Biomass}} = P_{\text{Ton}}^{\text{Biomass}} E_{\text{Barrel}}^{\text{Oil}} / E_{\text{Ton}}^{\text{Biomass}} \quad (1)$$

where

$Eq P_{\text{Barrel}}^{\text{Biomass}}$ = oil equivalent biomass purchase price (\$/barrel oil)

$P_{\text{Ton}}^{\text{Biomass}}$ = biomass purchase price (\$/dry Mg)

$E_{\text{Barrel}}^{\text{Oil}}$ = energy content of oil (GJ/barrel)

$E_{\text{Ton}}^{\text{Biomass}}$ = energy content of biomass (GJ/Mg)

Given that $E_{\text{Barrel}}^{\text{Oil}} = 6.13$ GJ/barrel and $E_{\text{Ton}}^{\text{Biomass}} = 17.2$ GJ/Mg, Equation (1) simplifies to $P_{\text{Ton}}^{\text{Biomass}}/2.8$. Thus for example the oil-equivalent purchase price of biomass in the range of \$60–80/dry metric ton is \$21–29/barrel, competitive with that of petroleum even at the low oil prices observed in 2016.

As summarized in Table 1, several pioneer facilities producing ethanol from lignocellulosic agricultural residues with capacity ≥ 10 million gallons per year have been built over the last few years. All of these facilities feature a dedicated process step in which cellulases and other saccharolytic enzymes are produced by aerobic fungi, and all feature pretreatment with heat, added chemicals, and often both—referred to here as thermochemical pretreatment. These facilities use yeast to produce ethanol with the exception of the DuPont facility, which uses *Zymomonas*. Pioneer cellulosic biofuel facilities are an important, long-awaited advance in the field because they allow (a) evaluation of costs and operability based on

experience rather than projection, and (b) realization of cost reductions driven by ‘learning by doing’.

High capital costs are an impediment to the cost-competitiveness and replication of pioneer cellulosic biofuels facilities. For example, while the capital cost per annual gallon of capacity averages \$13.81/annual gallon for the facilities listed in Table 1, the corresponding value for corn plants is on the order of \$2/gallon [9]. A capital cost of \$13.81/annual gallon corresponds to an annualized cost of \$2.76 per gallon ethanol, which exceeds the average market price of ethanol when oil was \$100/barrel (Table 2). Compared to the low prices seen in 2016, with oil at \$30/barrel, an annualized capital cost of \$2.76/gallon exceeds the market price of ethanol by about 1.8-fold and the price based on energy content by about fourfold. The cost of feedstock is not considered in these comparisons and is normally higher than the annualized cost of capital for economically viable production of commodity products such as fuels.

The cost of added cellulase enzymes per gallon ethanol is given by Equation (2):

$$C = LP/Y \quad (2)$$

where

C = cellulase cost (\$/gallon ethanol)

L = cellulase loading (mg protein/g feedstock = kg protein/metric ton feedstock)

P = cellulase price (\$/kg)

Y = ethanol yield (gallons/Mg).

Table 1

Pioneer facilities producing ethanol from lignocellulosic agricultural residues with capacity ≥ 10 million gallons per year

Company	Location	Feedstock	Scale (MGY)	CapEx (MM \$)	CapEx (\$)/Annual Gal	Coproducts	Sources
Abengoa	Kansas, USA	Corn stover, Straw	25	444.6	17.78	Heat, electricity	^b
Beta Renewables	Crescentino, Italy	Grass	13.4	171	12.76	Heat, electricity	^c
DuPont	Iowa, USA	Corn stover	30	500 ^a	16.67 ^a	Solid boiler fuel	^d
Granbio	Alagoas, Brazil	Bagasse, straw	21.6	265	12.27	Heat, electricity	^e
POET/DSM	Iowa, USA	Corn stover	20	275	13.75	Heat	^f
Raizen	Piracicaba, Brazil	Bagasse, straw	10.6	102	9.62	Heat, electricity	^{g,h}
Average			20.1	293	13.81		

^a DuPont CapEx includes feedstock supply infrastructure.

^b http://www.energy.gov/sites/prod/files/2015/04/f22/demonstration_market_transformation_bradford_3432.pdf.

^c <http://www.betarenewables.com/en/crescentino/the-project>.

^d <http://www.processingmagazine.com/duPont-defends-cellulosic-ethanol-plant-announces-laundry-detergent-deal/>.

^e http://www.granbio.com.br/en/wp-content/uploads/sites/2/2014/09/partida_english.pdf.

^f http://www.energy.gov/sites/prod/files/2015/04/f22/demonstration_market_transformation_ward_3433.pdf.

^g <http://www.raizen.com.br/en/energy-future/renewable-energy-technology/second-generation-ethanol>.

^h <https://www.bloomberg.com/news/articles/2013-03-13/raizen-to-spend-102-million-on-brazil-cellulosic-ethanol-plant>.

Table 2

Comparative prices for various fuels and capital costs for cellulosic ethanol

	Oil at \$100/barrel (Feb '12, July '13, Apr '14)	Oil at \$30/barrel (Mar '02, Jan '09, Mar '16)
Gasoline price		
Average Wholesale ^a	\$2.96/gal ± 0.03	\$1.04/gal ± 0.10
Corn ethanol price		
Average Market ^b	\$2.68/gal EtOH ± 0.44	\$1.57/gal EtOH ± 0.22
Gasoline equivalent (BTU basis) ^c	\$1.99/gal EtOH	\$0.70/gal EtOH
Cellulosic ethanol capital cost		
Total	\$293 million ^d	
Per annual gallon capacity	\$13.81 ^e	
Selling price contribution	\$2.76 ^f	

Fuel prices in 2015 dollars.

^a U.S. Department of Energy, Energy Information Administration, Independent Statistics & Analysis. (12/1/2016). *U.S. Regular Gasoline Rack Sales Price by Refiners*. Retrieved from https://www.eia.gov/dnav/pet/hist/LeafHandler.ashx?n=PET&s=EMA_EPMR_PRG_NUS_DPG&f=M.

^b USDA Economic Research Service, U.S. Bioenergy Statistics. (12/5/2016). *Table 14–Fuel ethanol, corn and gasoline prices, by month*. Retrieved from <https://www.ers.usda.gov/data-products/us-bioenergy-statistics/>.

^c Gasoline price*0.67.

^d Average from Table 1.

^e Average from Table 1.

^f Based on a capital recovery factor of 0.2, corresponding to a return on investment of about 16% depending on details of the schedule for construction and ramp up of capacity.

Based on the carbohydrate content of cellulosic biomass and typical process yields, 75 gallons per short ton (82.5 gallons per metric ton) is a reasonable value for Y for today's technology. At-site production of cellulase is expected to be less expensive than off-site production, but adds to process complexity and already high capital costs. More aggressive pretreatment can lower the required loading and hence cost of added enzymes, but is typically accompanied by higher costs elsewhere in the process. The cost of at-site enzyme production is estimated by Klein-Marcuschamer et al. [10] to be \$10/kg protein. Amylase enzymes produced via mature technology and purchased in large amounts by the corn ethanol industry are valued at about \$25/kg protein [11]. With $Y = 82.5$ gallons per ton and $P = \$15/\text{kg}$ protein, Equation (2) becomes $C = L/5.5$. At 10 mg cellulase protein/g dry solids, lower than most loadings in the research literature [11], the cost of cellulase is \$1.82 per gallon ethanol. If either L or P were halved, this becomes \$0.91/gallon. If both were halved, \$0.45/gallon—which is still a great deal for a product with an average recent (2014 through 2016) market price of \$2.22/gallon and average gasoline equivalent price of \$1.78/gallon in the US over the last 3 years.

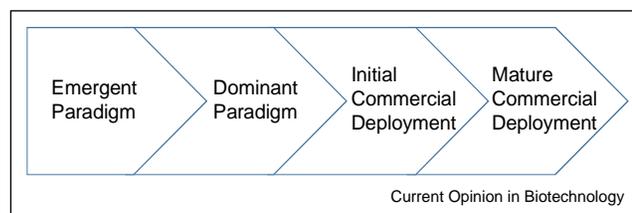
Clearly the main economic obstacle to cost-competitive cellulosic biofuel production is the cost of conversion rather than the cost of feedstock. The key factor responsible for the high cost of processing cellulosic biomass using current technology is the recalcitrance of lignocellulose, that is, the difficulty of its conversion to reactive intermediates [12,13,14*]. The recalcitrance barrier is manifested in costs associated with the two unit

operations aimed at rendering cellulosic biomass fermentable: thermochemical pretreatment and enzymatic hydrolysis.

Innovation

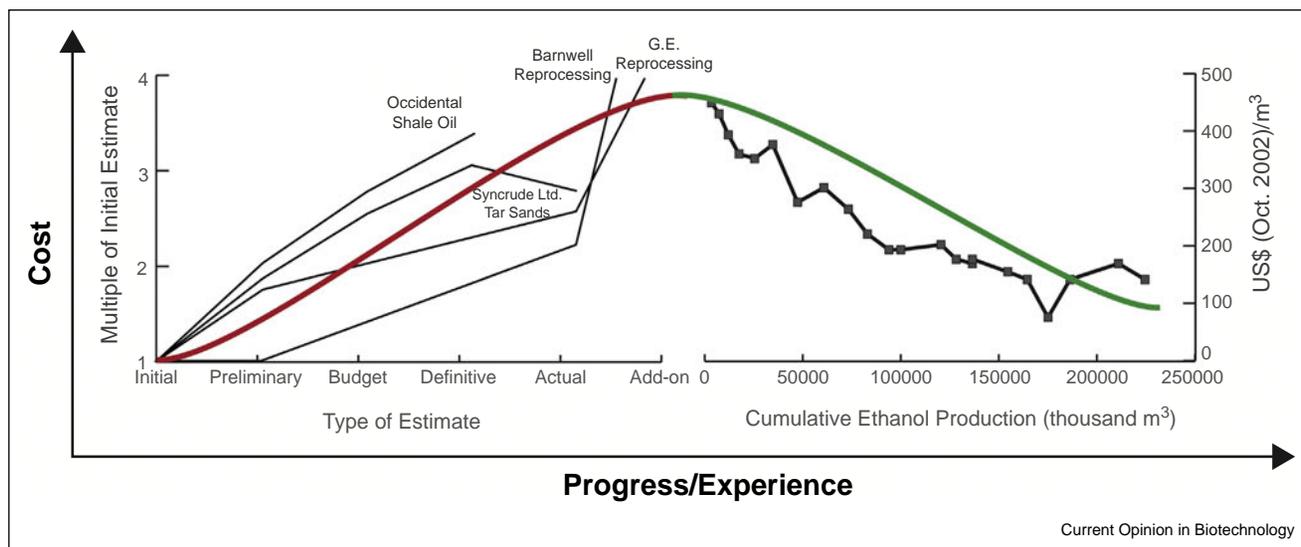
Adoption of new technologies involves a progression from an emergent paradigm, to a dominant paradigm, to initial commercial deployment, to mature deployment (Figure 1). For biomass processing technology, and some other technologies, it is often advantageous for initial commercial deployment to involve 'bolt-on' configurations at a host facility based on established technology that makes available feedstock and/or infrastructure at lower cost than would be the case for a stand alone facility. Examples include bagasse conversion to ethanol at a host facility processing sugar cane, and corn fiber conversion at a host facility processing corn kernels. In mature deployment, technological risk is minimized, the value of the once-new technology is maximized by integration into production facilities and the broader economy, and this technology bears its full share of infrastructure costs.

Figure 1



Stages of new technology adoption.

Figure 2



Innovation cost curve.

From a cost point of view, the progression in Figure 1 typically involves ascending costs as the first commercial application is approached, followed by descending costs informed by experience and innovation. Together these two trends define an innovation cost curve, illustrated in Figure 2 using results from the landmark Rand study [15] and cost reductions for cane ethanol production in Brazil [16]. The innovation cost curve applies to both new industries, and also new processing paradigms within those industries. Innovation can involve precommercial advancement of new paradigms and industries up the ascending part of the curve, or post commercial advancement down the descending part of the curve. Different processing paradigms have different ultimate potential to achieve low costs, although this potential cannot be known with certainty in advance of progressing through the innovation cost curve.

The thermochemical pretreatment/fungal cellulase paradigm has dominated the cellulosic biofuels field for over a quarter century. Given the recent emergence of pioneer cellulosic ethanol facilities based on this paradigm, it is likely that they are at the peak of the new technology cost curve. Cost reductions as a result of in-paradigm innovation can be confidently anticipated as seen for ethanol from both corn [17] and sugar cane [18]. Whether these cost reductions will be sufficient to provide the impetus for cellulosic biofuels to rapidly exceed the scale of current production from more easily-fermented feedstocks, as must occur in order for cellulosic biofuels to meaningfully impact climate objectives, is an open question. In light of the imperative to address climate change, the still high cost of cellulosic biofuel production via the thermochemical pretreatment/fungal cellulase paradigm,

the increased barrier-to-entry represented by low oil prices, and the emergence of promising alternatives, we believe that there is ample incentive to explore approaches outside the current processing paradigm. By way of illustration, one such approach is considered here: consolidated bioprocessing using thermophilic bacteria combined with milling during fermentation, termed cotreatment.

An illustrative example

Several cultures of thermophilic anaerobic bacteria [19^{••}], and in particular *Clostridium thermocellum* [20^{••}], have been recently shown to be markedly more effective at deconstructing cellulosic biomass than industry-standard fungal cellulase under a broad range of conditions. While not yet completely understood, the effectiveness of *C. thermocellum* at lignocellulose solubilization has been attributed to the ability to splay ends of cellulose fibers [21] and the presence of multiple cellulase modalities [22[•]]. *C. thermocellum* has also been shown to be capable of carrying out soluble sugar fermentation in the presence of aggressive ball milling, whereas yeast has not [23]. Wild-type strains of *C. thermocellum* and other thermophilic, saccharolytic anaerobes produce organic acids, in particular acetic acid, in addition to ethanol and do not exhibit high ethanol tolerance. The hemicellulose-fermenting *Thermoanaerobacterium saccharolyticum* has been engineered to produce ethanol at a yield of 0.46 g ethanol/g fermented sugar, comparable yields for hexose fermentation by yeast, and titers up to 70 g/L [24[•]], which is close to the upper limit of that feasible from cellulosic biomass given material handling constraints [25]. An engineered strain of *C. thermocellum* has recently been developed that

Table 3

Process scenarios				
	1. Base case	2. Base case + configurational changes	3. Base case + projected R&D advances	4. Advanced case
Thermochemical pretreatment	Dilute acid	Dilute acid	–	–
Cotreatment	–	–	Yes	Yes
Added cellulase	Produced at-site	Produced at-site	–	–
Coproduct	Electricity	Fuel pellets	Electricity	Fuel pellets
Boiler type	Solid fuel	Gas	Solid fuel	Gas
Wastewater treatment	Aerobic + anaerobic	Aerobic + anaerobic	Anaerobic	Anaerobic
External process energy source	–	Electricity	–	Natural gas and electricity

produces ethanol at 75% of theoretical yield and a titer of 25 g/L [26^{*}].

Informed by these results, we analyze here futuristic process scenarios involving conversion of corn stover to ethanol using thermophilic fermentation in a consolidated bioprocessing (CBP) configuration with no added enzymes and with milling during fermentation, termed cotreatment, in lieu of thermochemical pretreatment. Our purpose in undertaking this analysis and comparison is to explore what could be possible in the future assuming R&D-driven improvements that have not yet been realized. Table 3 defines the scenarios examined. Parameters used in the analysis of these scenarios are presented in Tables S.1 and S.2. All results are in 2014 dollars.

Scenario 1, the base case, is the most recent published NREL design using dilute acid hydrolysis, fungal cellulase addition, and fermentation with *Zymomonas mobilis* as reported by Humbird *et al.* [27^{*}] except with a lower cost for anaerobic digestion (see Table S.1). Scenarios 2 through 4 assume the same feedstock flow as for Scenario 1, 2756 U.S. tons per day at 20% moisture, producing about 60 million gallons of ethanol per year. Scenario 2 is the base case with two configurational changes: production of fuel pellets in lieu of electricity as a coproduct, and use of gas boilers in lieu of a solid fuel boiler. Scenario 3 is the base-case with R&D-driven advances: thermophilic fermentation with no added enzyme in lieu of *Z. mobilis* fermentation with added cellulase, and cotreatment in lieu of pretreatment. The Advanced case, Scenario 4, includes both configurational changes and R&D-driven advances. Whereas aerobic treatment including a nitrogen removal step is included in Scenarios 1 and 2 in order to treat effluents resulting from dilute acid pretreatment, only anaerobic wastewater treatment is included in cases 3 and 4 since the latter cases do not add ammonia for pretreatment hydrolyzate conditioning and thus do not need to remove nitrogen. Scenarios 1 and 3 derive process steam and electricity, as well as exported electricity, from process residues. In Scenarios

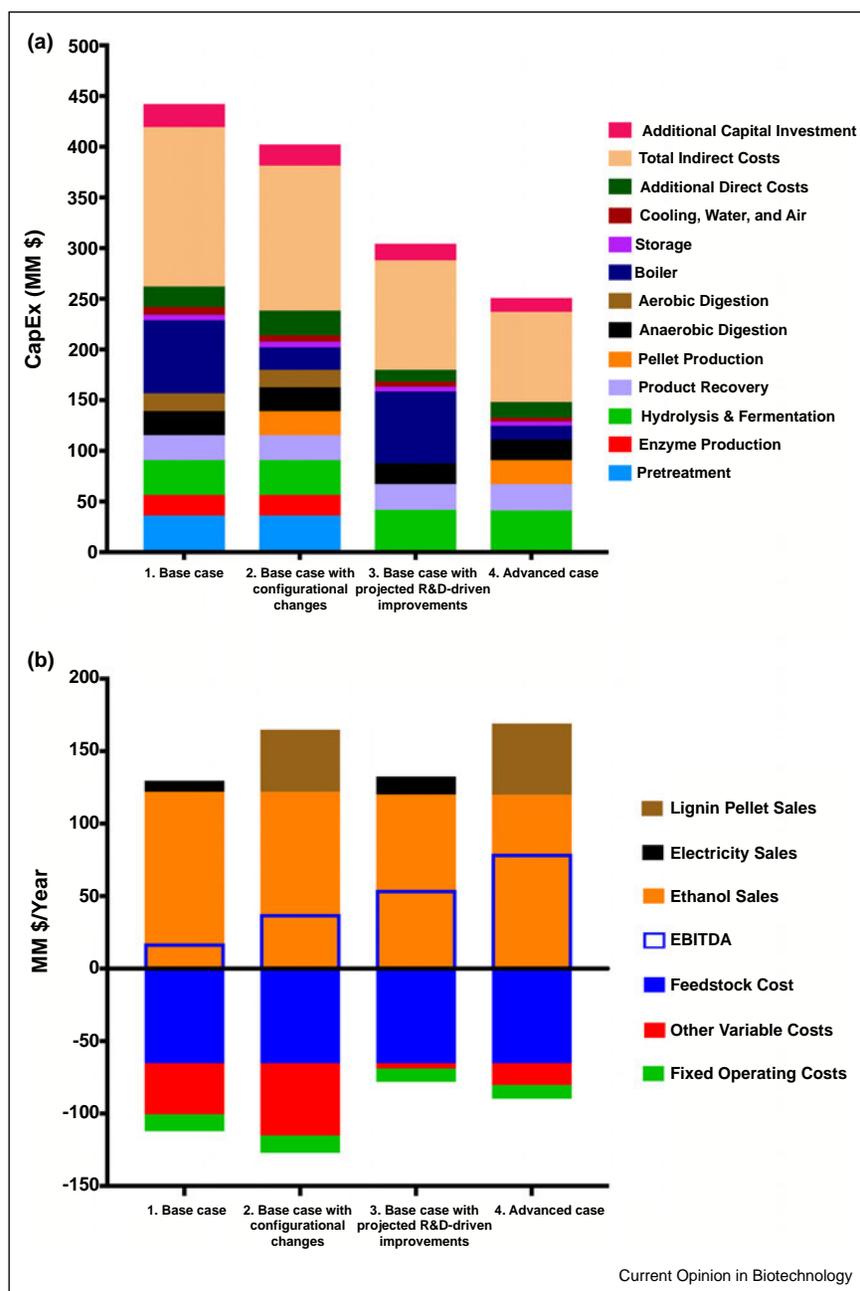
2 and 4, external electricity is supplied to the process. For Scenario 2, methane from anaerobic digestion is sufficient to meet process steam requirements. For Scenario 4, methane from anaerobic digestion is supplemented by natural gas. R&D advances needed to fully realize the performance assumed for Scenarios 3 and 4 are associated with developing thermophiles into robust biocatalysts, and in particular achieving high ethanol yields and titers at high solids loading with a cost-effective growth medium. Progress pursuant to these goals has recently been reviewed [20^{**}].

Capital and operating costs are progressively lower for Scenarios 1 through 4, as shown in Figure 3a and b, respectively. Annual earnings before interest, taxes, depreciation, and amortization (EBITDA), a measure of net revenue, increases markedly from \$17.4 million per year for Scenario 1 to \$37.7 million, \$54.3 million, and \$79.2 million for Scenarios 2, 3, and 4 respectively.

The ratio of capital costs to EBITDA has units of years and can be interpreted as a payback period. Figure 4 presents the payback period for Scenarios 1 through 4 as a function of plant scale (MM gallons per year). Progressing from Scenarios 1 through 4, the payback period is markedly lower at all scales. The other notable feature is the much-reduced sensitivity of payback period to scale for Scenarios 3 and 4 compared to Scenarios 1 and 2. Table S.3. presents a sensitivity analysis of the payback period to various process parameters. High sensitivity is observed with respect to feedstock and ethanol price, with more modest sensitivity exhibited for the price of pellets and electricity, total capital cost, and energy and capital for cotreatment. The energy requirement for cotreatment has not been determined, and is judged to have the largest uncertainty of the parameters evaluated in Table S.3.

Energy flows are presented for Scenarios 1 through 4 in Figure 5. Ethanol represents about 40% of the energy (lower heating value basis) in the entering feedstock in all

Figure 3



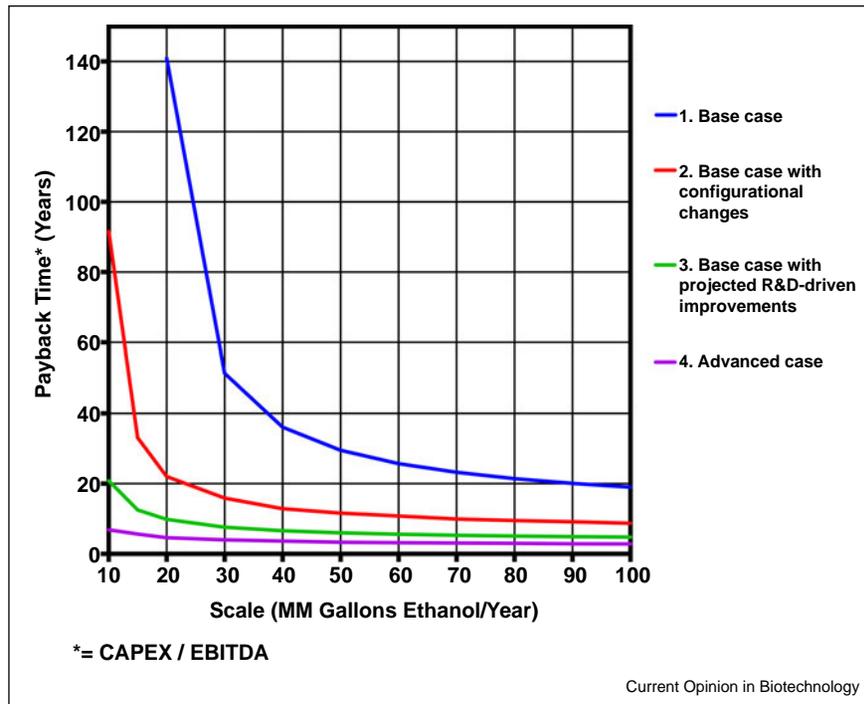
(a) Capital cost summary. Values shown are installed costs for the components listed. Indirect capital costs include proratable expenses, field expenses, home office and construction fees, project contingency, start-up, and permits. (b) Operating costs, revenue, and EBITDA. Other variable costs include chemicals used in pretreatment and neutralization (sulfuric acid, ammonia), nutrients for microbial production of ethanol and cellulase, purchased energy (for Scenarios 2 and 4), boiler chemicals and ash disposal.

Scenarios. Net electricity exports are 3.4% and 5.5% of feedstock energy for Scenario 1 and 3. For Scenarios 2 and 4, energy exported as pellets are 35.2% and 39.0% of feedstock energy respectively. Imported electricity is 7.5% of the feedstock energy for Scenario 2 and 4.6% for Scenario 4. Imported natural gas is 5.3% of feedstock energy for Scenario 4. Three quarters of the steam

demand is provided by biogas in Scenario 4. Imported natural gas might be eliminated in configurations with a greater degree of heat integration.

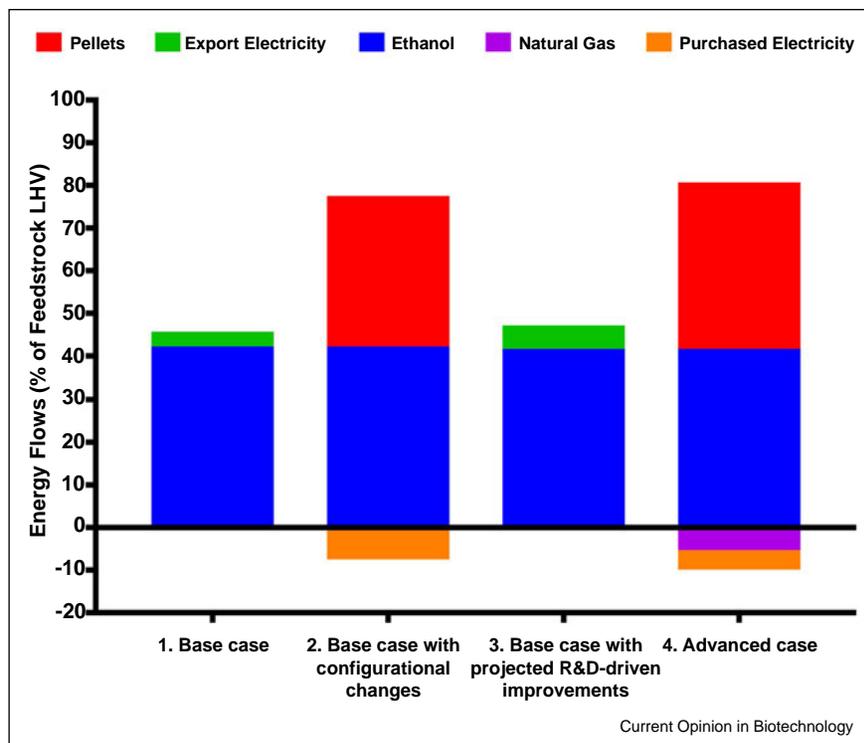
Net lifecycle greenhouse gas mitigation according to the 2016 GREET[®] model [28] is presented in Figure 6 for Scenarios 1 and 4, with assumptions as listed in Note S.A.

Figure 4



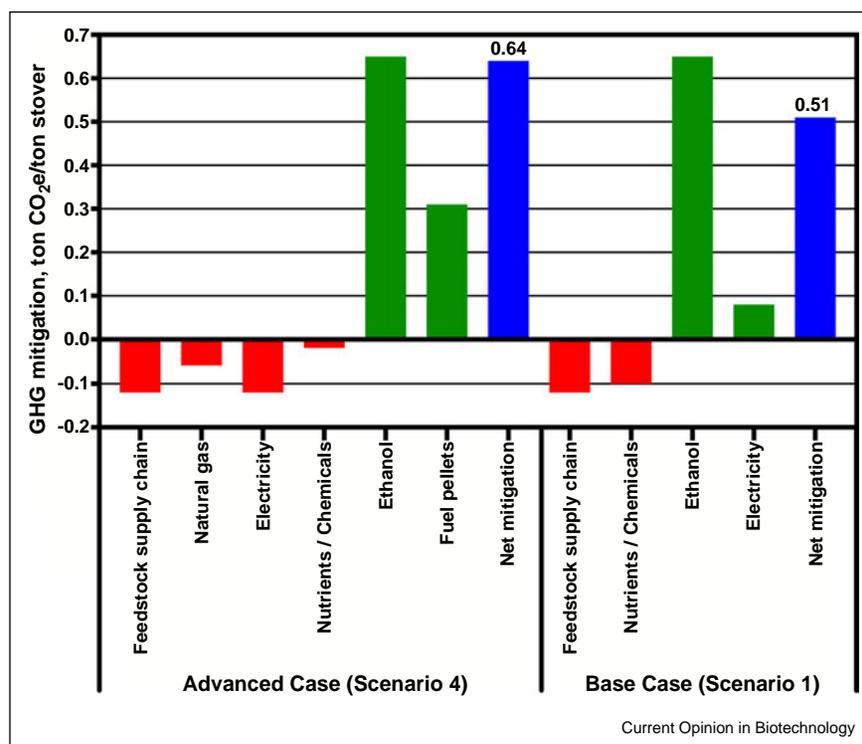
Payback time in relation to scale.

Figure 5



Energy flows.

Figure 6



Comparative greenhouse gas mitigation for Scenarios 1 and 4.

As shown in the figure, the emission benefits of fuel pellet production more than offset the emissions from imported natural gas and electricity for Scenario 4.

Discussion

Biological production of cellulosic biofuels involves 'upstream' technologies that convert lignocellulose to fermentable carbohydrate and 'downstream' technologies that convert fermentable carbohydrate to fuels [29]. Innovation targeting upstream process steps is needed to address the recalcitrance barrier common to all molecules derived from cellulosic biomass. Innovation targeting downstream process steps is needed to produce a diversity of molecules and thereby enable various transport applications and coproduct opportunities. In order to prevent risk from becoming unacceptably high, it is necessary to avoid commercial deployment of too many new technologies at once. Consistent with this, new upstream cellulosic biofuel technologies will likely be proven and deployed first in conjunction with established downstream technologies, for example at facilities producing ethanol or bioelectricity. New downstream technologies will likely be proven and deployed first in conjunction with established upstream technologies, for example facilities processing corn or sugar cane. For both types of innovation, deployment in a bolt-on mode at existing industrial facilities is likely to be initially

advantageous. These trends are evident within the emergent advanced biofuel field.

Innovation within the thermochemical pretreatment/fungal cellulase paradigm – for example targeting solids delivery, new pretreatment chemistries, and improved cellulase preparations – is necessary in order to support and accelerate the replication of costly pioneer facilities. New paradigm innovation offers potential for transformative cost reductions which may well be necessary in order for cellulosic biofuels to be widely cost-competitive in stand-alone facilities, but requires targeted investment lest it always be in the distant future. As new paradigm innovations progress through the innovation cost curve (Figure 2), their estimated costs can be expected to rise and then fall. Some will encounter liabilities or limitations that prevent them from being competitive with established processes; others will realize the originally anticipated potential and will displace earlier technologies.

Keeping in mind the uncertainties inherent in forecasting new-paradigm innovation, the results presented herein for consolidated bioprocessing using thermophilic bacteria combined with cotreatment, referred to as CBP/CT, are instructive. The radical cost reduction potential of the Advanced scenario (Figure 4) stems from a combination of configurational changes and R&D-driven advances,

with both contributing significantly but the latter having greater economic impact than the former. The key configurational changes evaluated were the coproduction of fuel pellets in lieu of electricity and use of natural gas boiler(s) in lieu of a solids boiler. These alterations decrease CapEx modestly (Figure 3a); substantially increase EBITDA (Figure 3b) and thermodynamic efficiency (Figure 5); substantially reduce the payback period (Figure 4); and appear relatively robust to changes in the price of pellets and electricity (Table S.3). The key R&D-driven advances evaluated, CBP/CT in lieu of thermochemical pretreatment and fungal cellulase addition, decrease CapEx substantially (Figure 3a), increase EBITDA (Figure 3b), and substantially reduce the payback period (Figure 4). At a scale of 2756 tons of corn stover per day and compared to the Base case scenario, the Advanced case has 43% lower capital costs, 4.6 fold higher EBITDA, eightfold shorter payback period, and 25% higher displaced greenhouse gas emissions per ton biomass. The cost estimates presented are for a stand-alone CBP/CT facility. Deployment in a bolt-on mode is expected to offer cost advantages compared to a stand-alone facility, which would foster commercial application in advance of full realization of the performance parameters assumed here (Table S.2).

The sensitivity of payback period with respect to scale is markedly lower for all scenarios, and particularly Scenarios 3 and 4, compared to the base case. Operation at smaller scale offers several important advantages, most of which are not captured in the analysis presented here. These include lower feedstock cost, easier plant siting and integration into local land use and material flows, lower total capital cost, and thus more rapid replication and faster learning. Smaller, less capital-intensive plants are consistent with anticipated trends and opportunities in biomanufacturing [30].

Cellulosic ethanol has an important role to play as a proving ground for new technologies. Once low-cost 'front end' technology is established, product diversification to other fuel molecules and coproducts can readily be anticipated as has been observed for the petroleum [31], coal [32], and corn processing industries [33]. Consolidated bioprocessing with cotreatment provides a powerful, although still speculative, example of the potential benefits of including new-paradigm as well as in-paradigm innovation in R&D portfolios.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.copbio.2017.03.008>.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. **Fulton LM, Lynd LR, Körner A, Greene N, Tonachel LR: The need for biofuels as part of a low carbon energy future.** *Biofuels, Bioprod. Biorefin.* 2015, **9**:476-483.
Biofuels will likely be required in order to decarbonize about half of anticipated global transport energy demand according to the IEA two degree scenario.
2. **Souza GM, Victoria RL, Verdade LM, Joly CA, Netto PEA, Cantarella H, Chum HL, Diaz-Chavez R, Fernandes E, Fincher G et al.: Bioenergy numbers.** In *Bioenergy & Sustainability: Bridging the Gaps*. Edited by Souza GM, Victoria RL, Joly CA, Verdade LM. Paris: SCOPE; 2015:28-57.
Bioenergy Numbers is a useful compilation of information within a comprehensive report addressing various aspects of bioenergy merit and potential.
3. **Jordan N, Boody G, Broussard W, Glover JD, Keeney D, McCown BH, McIsaac G, Muller M, Murray H, Neal J et al.: Sustainable development of the agricultural bio-economy.** *Science* 2007, **316**:1570-1571.
4. **Werling BP, Dickson TL, Isaacs R, Gaines H, Gratton C, Gross KL, Liere H, Malmstrom CM, Meehan TD, Ruan L et al.: Perennial grasslands enhance biodiversity and multiple ecosystem services in bioenergy landscapes.** *Proc. Natl. Acad. Sci. U.S.A.* 2014, **111**:1652-1657.
5. **Lynd LR, Sow M, Chimphango AF, Cortez LA, Brito Cruz CH, Elmissiry M, Laser M, Mayaki IA, Moraes MA, Nogueira LA et al.: Bioenergy and African transformation.** *Biofuels Biotechnol.* 2015, **8**:18.
An exploration of the potential for realizing social benefits via bioenergy in Africa, informed by experience in Brazil.
6. **Anderson JE, Diccio DM, Ginder JM, Kramer U, Leone TG, Raney-Pablo HE, Wallington TJ: High octane number ethanol-gasoline blends: quantifying the potential benefits in the United States.** *Fuel* 2012, **97**:585-594.
7. **Thomas JF, West BH, Huff SP: Effects of High-octane Ethanol Blends on Four Legacy Flex-fuel Vehicles, and a Turbocharged GDI Vehicle.** 2015. ORNL/TM-2015/116.
Addresses the potential to use ethanol in high-efficiency engines.
8. **Crooks E: The US Shale Revolution.** *Financ. Times*; 2015.
9. **Cardno ENTRIX: Current State of the US Ethanol Industry.** 2010. DOE Subcontract 02, http://www1.eere.energy.gov/bioenergy/pdfs/current_state_of_the_us_ethanol_industry.pdf.
10. **Klein-Marcuschamer D, Oleskowicz-Popiel P, Simmons BA, Blanch HW: The challenge of enzyme cost in the production of lignocellulosic biofuels.** *Biotechnol. Bioeng.* 2012, **109**:1083-1087.
11. **Stephen JD, Mabee WE, Saddler JN: Will second-generation ethanol be able to compete with first-generation ethanol? Opportunities for cost reduction.** *Biofuels, Bioprod. Bioref.* 2012, **6**:159-176.
12. **Lynd LR, Wyman CE, Gerngross TU: Biocommodity engineering.** *Biotechnol. Prog.* 1999, **15**:777-793.
13. **Himmel ME, Ding S-Y, Johnson DK, Adney WS, Nimlos MR, Brady JW, Foust TD: Biomass recalcitrance: engineering plants and enzymes for biofuels production.** *Science* 2007, **315**:804-807.
14. **U.S. Department of Energy: Lignocellulosic Biomass for Advanced Biofuels and Bioproducts: Workshop Report.** 2015. DOE SC-0170.

An examination of the scientific barriers to expanding the bioeconomy based on lignocellulosic feedstocks, including recognition of the continuing importance of the recalcitrance barrier as an impediment to cost-competitive production.

15. Merrow EW, Chapel SW, Worthing C: *A Review of Cost Estimation in New Technologies*. RAND Corporation; 1979.
 16. Goldemberg J, Coelho ST, Nastari PM, Lucon O: **Ethanol learning curve—the Brazilian experience**. *Biomass Bioenergy* 2004, **26**:301-304.
 17. Hettinga WG, Junginger HM, Dekker SC, Hoogwijk M, McAloon AJ, Hicks KB: **Understanding the reductions in US corn ethanol production costs: an experience curve approach**. *Energy Policy* 2009, **37**:190-203.
 18. van den Wall Bake JD, Junginger M, Faaij A, Poot T, Walter A: **Explaining the experience curve: cost reductions of Brazilian ethanol from sugarcane**. *Biomass Bioenergy* 2009, **33**:644-658.
 19. Paye JMD, Guseva A, Hammer SK, Gjersing E, Davis MF,
 - Davison BH, Olstad J, Donohoe BS, Nguyen TY, Wyman CE *et al.*: **Biological lignocellulose solubilization: comparative evaluation of biocatalysts and enhancement via cotreatment**. *Biotechnol. Biofuels* 2016, **9**:8.

A controlled comparison of lignocellulose solubilization involving six biocatalysts and three feedstocks, including an initial report of cotreatment to augment fermentation by *Clostridium thermocellum*.
 20. Lynd LR, Guss AM, Himmel ME, Beri D, Herring C, Holwerda EK,
 - Murphy SJ, Olson DG, Paye J, Rydzak T *et al.*: **Advances in consolidated bioprocessing using *Clostridium thermocellum* and *Thermoanaerobacter saccharolyticum***. In *Industrial Biotechnology: Microorganisms*. Edited by Wittmann C, Liao JC. Wiley-VCH Verlag GmbH & Co. KGaA; 2017:365-394.

Comprehensive comparative data is presented indicating that *C. thermocellum* achieves 2- to 4-fold higher solubilization than industry-standard fungal cellulase on minimally-pretreated lignocellulose feedstocks. Recent progress at engineering two thermophilic anaerobes for improved ethanol production is also reviewed.
 21. Resch MG, Donohoe BS, Baker JO, Decker SR, Bayer EA, Beckham GT, Himmel ME: **Fungal cellulases and complexed cellulosomal enzymes exhibit synergistic mechanisms in cellulose deconstruction**. *Energy Environ. Sci.* 2013, **6**:1858-1867.
 22. Xu Q, Resch MG, Podkaminer K, Yang S, Baker JO, Donohoe BS,
 - Wilson C, Klingeman DM, Olson DG, Decker SR *et al.*: **Dramatic performance of *Clostridium thermocellum* explained by its wide range of cellulase modalities**. *Sci. Adv.* 2016, **2**:e1501254.

The latest perspectives on the mechanistic basis for the effectiveness of *C. thermocellum* at mediating solubilization of lignocellulosic feedstocks.
 23. Balch ML, Holwerda EK, Davis M, Sykes R, Happs R, Kumar R, Wyman CE, Lynd LR: **Lignocellulose fermentation and residue characterization for senescent switchgrass fermentation by *Clostridium thermocellum* in the presence and absence of continuous in-situ ball-milling**. *Energy Environ. Sci.* 2017 <http://dx.doi.org/10.1039/C6EE03748H>.
 24. Herring CD, Kenealy WR, Joe Shaw A, Covalla SF, Olson DG,
 - Zhang J, Ryan Sillers W, Tsakraklides V, Bardsley JS, Rogers SR *et al.*: **Strain and bioprocess improvement of a thermophilic anaerobe for the production of ethanol from wood**. *Biotechnol. Biofuels* 2016, **9**:125.

Production of ethanol at commercially viable yields and titers is reported for engineered strains of a hemicellulose-fermenting thermophilic anaerobe.
 25. Lynd LR, Weimer PJ, van Zyl WH, Pretorius IS: **Microbial cellulose utilization: fundamentals and biotechnology**. *Microbiol. Mol. Biol. Rev.* 2002, **66**:506-577.
 26. Tian L, Papanek B, Olson DG, Rydzak T, Holwerda EK, Zheng T, Zhou J, Maloney M, Jiang N, Giannone RJ *et al.*: **Simultaneous achievement of high ethanol yield and titer in *Clostridium thermocellum***. *Biotechnol. Biofuels* 2016, **9**:116.
- A recent report of metabolic engineering of *Clostridium thermocellum* for improved ethanol production.
27. Humbird D, Davis R, Tao L, Kinchin C, Hsu D, Aden A, Schoen P,
 - Lukas J, Olthof B, Worley M *et al.*: *Process Design and Economics for Biochemical Conversion of Lignocellulosic Biomass to Ethanol: Dilute-Acid Pretreatment and Enzymatic Hydrolysis of Corn Stover*. 2011. DOE report NREL/TP-5100-47764.

The most recent published lignocellulose-to-ethanol process design by the National Renewable Energy Laboratory.
 28. Systems Assessment Group: *Energy Systems Division, Argonne National Laboratory, Summary of Expansions, Updates, and Results in GREET*. 2016.
 29. Lynd LR, Laser MS, Bransby D, Dale BE, Davison B, Hamilton R, Himmel M, Keller M, McMillan JD, Sheehan J *et al.*: **How biotech can transform biofuels**. *Nat. Biotechnol.* 2008, **26**:169-172.
 30. Clomburg JM, Crumbley AM, Gonzalez R: **Industrial biomanufacturing: the future of chemical production**. *Science* 2017, **355**.
 31. Congressional Research Service, Pirog R: *Petroleum Refining: Economic Performance and Challenges for the Future*. 2007. RL32248.
 32. Lynd LR, Von Blottnitz H, Tait B, De Boer J, Pretorius IS, Rumbold K, Van Zyl WH: **Converting plant biomass to fuels and commodity chemicals in South Africa: a third chapter?** *S. Afr. J. Sci.* 2003, **99**:499-507.
 33. Lynd LR, Wyman C, Laser M, Johnson D, Landucci R: *Strategic Biorefinery Analysis: Review of Existing Biorefinery Examples*. 2005. NREL/SR-510-34895.