How biotech can transform biofuels

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For cellulosic ethanol to become a reality, biotechnological solutions should focus on optimizing the conversion of biomass to sugars.

Enthusiasm for using biotech to meet societal energy challenges is at levels not seen since the early 1980s[1–5], when understanding and capability in the life sciences were at a radically different stage of development than today. Production of ethanol and other biofuels from cellulosic biomass is a major focus, with additional biotechnological paths to producing energy also receiving attention. The proposition that energy can be obtained from biomass with a decisively positive energy balance[6–8] and at a scale sufficiently large to have a substantial impact on sustainability and security objectives is both supported by several recent studies[8–11] and much more widely accepted now than only a few years ago. There is also increasing recognition of the potential for environmental benefits—including greenhouse gas mitigation, improved soil fertility and water quality, and improved wildlife habitat—if cellulosic crops were to be incorporated into the agricultural landscape[9,12]. Both government and industry are making unprecedented investments in the energy biotech field[1,3,4], and US president George W. Bush has mentioned cellulosic ethanol in two successive State of the Union speeches. Investment in energy technology startups in 2006 was twice that in 2005 and ten times that in 1999 (ref. 13) with energy biotech accounting for a substantial fraction[4].

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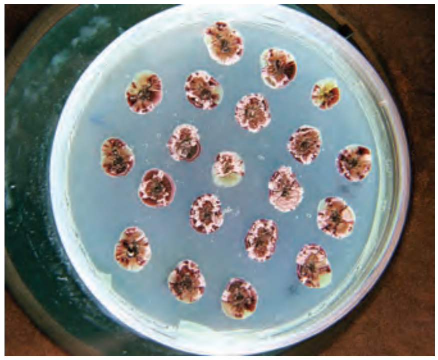
In response to this markedly increased activity and sense of potential, many new to energy biotech are looking for ways to bring their resources and expertise to bear in the field. This is appropriate because realizing even a fraction of the anticipated benefits of biomass energy will require manpower, investment, innovation and technology deployment on a vastly larger scale than seen to date.

With pressing needs to be met, high levels of investment, high expectations and many new players, it is critically important to develop a clear understanding of the central challenges that must be addressed to achieve more widespread bioenergy use. Research and development directed at this goal will require an integrated and interdisciplinary approach melding aspects of biology, process engineering and a variety of disciplines related to crop production and land use.

Here, we present an analysis of the economics of bioethanol production to identify the key steps in conversion of cellulosic biomass into liquid fuel that limit cost effectiveness. In particular, we identify the initial conversion of biomass into sugars as a key bottleneck in the process of biofuel production that will require new biotechnological solutions to improve efficiency.



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New types of recombinant bacteria (such as these cellulase producing streptomycetes) are needed to address the bottleneck in conversion of cellulosic biomass into sugars for fermentation.

Business and technology drivers

Pharmaceutical applications gave birth to modern biotech, which today generates nearly $50 billion annually[14]. Although the life-science tools and understanding that form the foundation of energy biotech are similar to those underlying the pharmaceutical industry, business and technology drivers for the energy biotech field have more in common with the oil and gas industry. The functionally similar products of energy biotech and the oil and gas industry are produced in very large amounts at low unit value with competitiveness determined primarily by the cost of raw materials and manufacturing. Raw material supply is a key concern for both energy biotech and the oil and gas industry, with scale and land-use implications important for energy biotech, and security, carbon emissions and long-term depletion important for oil and gas.

In contrast, biopharmaceutical production involves small amounts of products with very high unit value, raw material is not difficult to obtain and the cost of manufacturing and raw materials is typically a small contributor to selling price. Because production takes place on a small scale, environmental considerations become important for biopharmaceutical manufacturing only in the case of an accident or mismanagement, whereas such considerations are major strategic factors for both energy biotech and oil or gas production, even when processes are operating as designed. The anticipated progression of biotech from high-value, low-volume products to energy production parallels the development of the semiconductor industry, which began with aerospace applications before it became pervasive in high-volume consumer products.

Biomass feedstocks

Table 1 compares the value of various potential energy sources in commonly reported units and in $/gigajoule (GJ). Cellulosic biomass at $50/metric tonne is less expensive than all sources listed except coal, and it is advantageously priced relative to coal if the anticipated cost of carbon sequestration is included. At $50/tonne ($3/GJ), the purchase price of cellulosic biomass on an energy basis is the same as oil at $17/barrel (calculation details in **Supplementary Note** online).

In addition to being available at low cost, biomass feedstocks must also be available on a very large scale to have a meaningful impact on energy and sustainability challenges. Given finite land resources and competing land uses, the 'land fuel yield' (GJ fuel per hectare (ha) per year) is a critical variable affecting the achievable scale of bioenergy production. On the basis of current production data for corn and soy and estimated current productivity of biomass energy crops such as switchgrass[10], the potential land fuel yield from cellulosic biomass production (135 GJ/ha) is somewhat higher than for corn kernels (85 GJ/ha), whereas biodiesel from soy oil (18 GJ/ha) is dramatically lower than from either cellulosic biomass or corn (**Supplementary Note**).

Future improvements in crops and cropping systems can be expected to substantially increase the land fuel yield for these and other crops. For example, energy crop firm Ceres (Thousand Oaks, CA, USA) projects that average productivity of cellulosic energy crops of 15 tons per acre (roughly three times current productivity for switchgrass[15]) can be achieved across a broad range of geographic and climate regions—including most of the continental United States—in ten years, given an aggressive effort using modern breeding technologies. It is widely recognized that production of cellulosic crops, such as perennial grasses, short rotation trees or winter cover crops, could have substantially more positive environmental attributes than production of corn, soy or other annual row crops[6,7,9].

Consistent with the advantages of cellulosic feedstocks in terms of purchase price, potential fuel yield and environmental attributes, all scenarios known to us that foresee energy production from biomass on a scale sufficient to have large impacts on energy sustainability and security rely primarily on cellulosic biomass. Although the desirable features of cellulosic biomass as a bioenergy feedstock are well known, biofuel production by fermentation is based today on plant feedstocks, from which sugars are more easily obtained, such as corn and sugarcane. The cost of processing corn to sugar adds a modest amount to the feedstock carbohydrate cost with or without consideration of coproducts (**Fig. 1**). In contrast, the current cost of converting cellulosic biomass to sugar roughly doubles the carbohydrate purchase cost, eliminating the cost advantage of cellulosic biomass relative to corn at prices seen in the United States in recent years. The substantial potential benefits of large-scale energy production from cellulosic feedstocks will be difficult to realize until sugars can be produced from these feed-

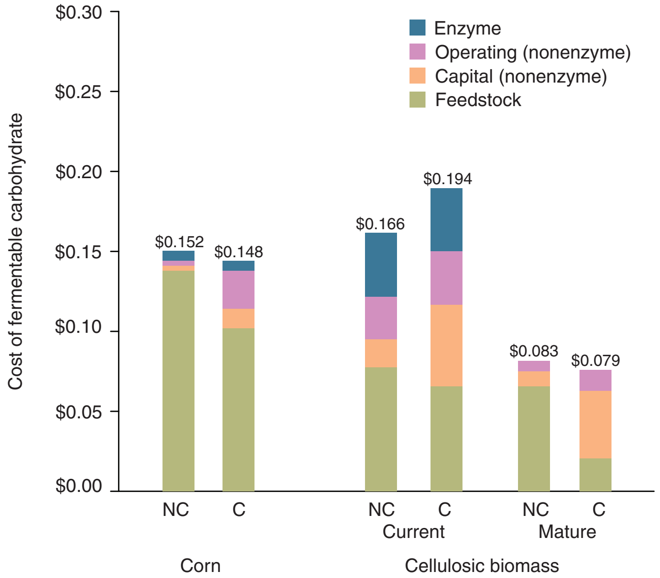

Figure 1 Cost of fermentable carbohydrate for processing corn and cellulosic biomass. Plant scale: corn, 2,544 dry ton/day (100 one-hundred-million gallons (MMgal) ethanol/year); current cellulosic biomass, 2,205 dry tons/day (60 MMgal/year); mature cellulosic biomass 5,000 dry tons/day (184 MMgal/year). Cost of corn = $2.33/bushel (average annual US price, 2001–2006; ref. 19). Cost of cellulosic biomass = $50/dry ton. Corn dry mill processing costs based on Wallace *et al.*[20]. NC, no coproducts; C, with coproducts.

Table 1 Prices of selected energy sources

Energy source	Price	
	Common ($/amount)	$/GJ[a]
Petroleum	50/bbl	8.7
Gasoline[b]	1.67/gallon	13.7
Natural gas[c]	7.50/scf	7.9
Coal[d]	20/ton	0.9
Coal with carbon capture[e,f]	106/ton	4.8
Electricity	0.04/kWh	11.1
Soy oil[g]	0.23/lb	13.8
Corn kernels[h]	2.30/bu	6.6
Cellulosic crops[i]	50/ton	3.0

[a]Assumed lower heating values: petroleum, 5.8 GJ/bbl; gasoline, 5.1 GJ/bbl; natural gas, 37.3 MJ/m^3; coal, 23.3 MJ/kg; soy oil, 36.8 MJ/kg; corn kernels, 16.3 MJ/kg; cellulosic crops, 17.4 MJ/kg. [b]Wholesale price, average 2004–2006 (ref. 21). [c]2005 annual average US wellhead price[21]. [d]2004 annual average US open market price[21]. [e]Cost of carbon capture assumed to be $150/ton carbon[22]. [f]Coal carbon content assumed to be 57% (dry weight basis)[23]. [g]Average price 2004–2005 (ref. 19). [h]Average price 2002–2005 (ref. 24). [i]Price representative of typical values assumed for energy crops in the literature (for example, McLaughlin *et al.*[25]). bbl, barrel; scf, standard cubic foot.

stocks at a cost competitive with production from corn and other more readily processed raw materials.

Biomass processing

To assess their importance for energy biotech, we consider below the impact of several R&D-driven improvements for ethanol production from cellulosic biomass. The processes considered here feature biological conversion and include the following steps: feedstock handling, pretreatment, biological conversion, product recovery, utilities production and waste treatment. Two reference scenarios—one using current technology, and another featuring advanced processing—are presented to give an indication of the sensitivity of cost-reduction estimates with respect to the process context considered.

Scenario 1, based on current technology, represents what can reasonably be expected to be achievable within a relatively short time (e.g., <one year) assuming resources are available for near-term development work. The design used is based on the analysis of Wooley *et al.*[16] with updated parameters reflecting progress in the field. Key unit operations include dilute acid pretreatment, on-site cellulase production, simultaneous saccharification and fermentation with separate fermentation of pentose sugars, evaporative concentration of liquid distillation bottoms and water recycle before wastewater treatment (**Fig. 2a**).

Scenario 2 illustrates what may be possible incorporating advanced nonbiological steps into the process. Process steps that are not biologically mediated (materials handling and receiving, pretreatment, distillation, utilities and waste treatment) are those projected for mature technology by Greene *et al.* (ref. 9 and unpublished data). Important advances in nonbiological processes include ammonia fiber expansion pretreatment, energy-saving distillation by an intermediate heat pump and optimal sidestream return and wastewater treatment using attached film anaerobic digestion (**Fig. 2b**). To enable evaluation of biotechnological improvements relative to a common baseline, the configuration and performance of biologically mediated process steps (enzyme production, simultaneous saccharification and fermentation, pentose fermentation) are the same for scenarios 1 and 2.

Relative to scenario 1, scenario 2 has a substantially larger scale, pretreatment by ammonia fiber expansion at a solids:water ratio of 2:1 instead of dilute acid at a solids:water ratio of 0.4, energy recovery from wastewater by anaerobic digestion instead of multi-effect evaporation and more advanced energy integration, including but not limited to heat pump–assisted distillation (performance parameters for these process scenarios are presented in the **Supplementary Note**).

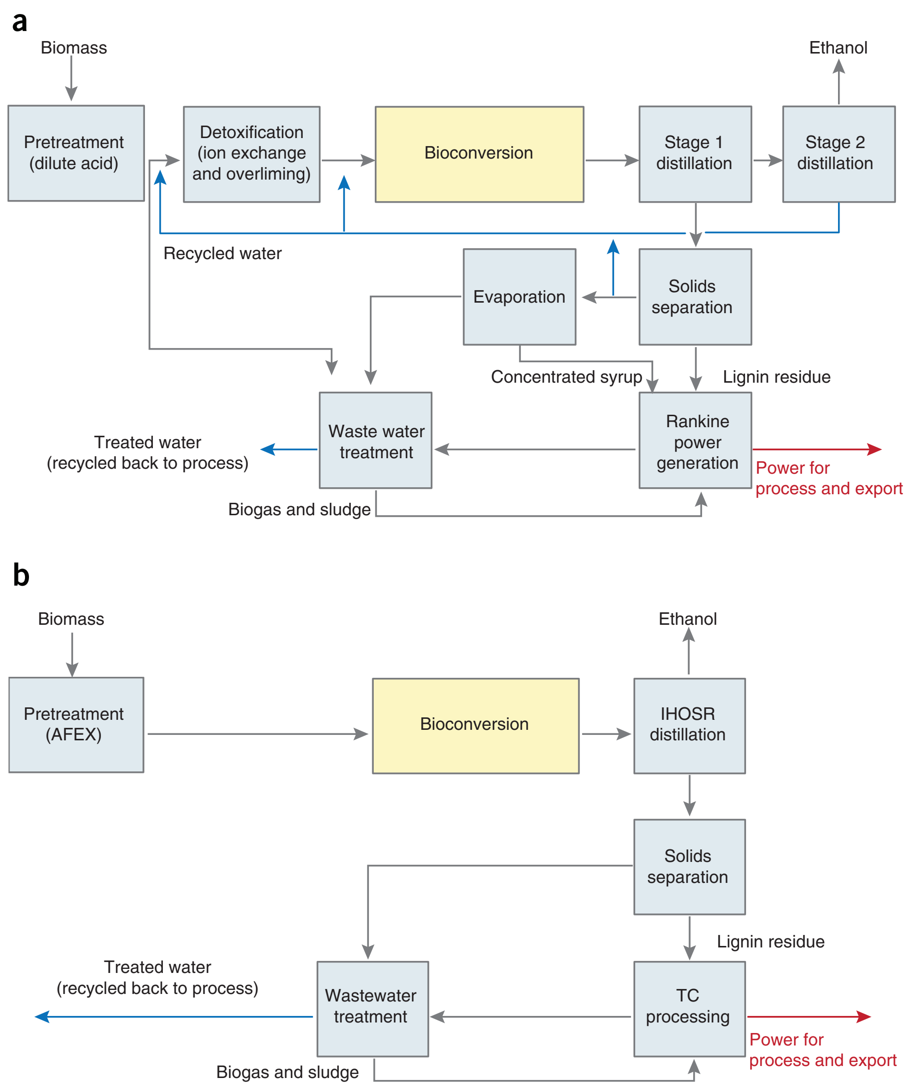

Figure 2 Biofuel production processes. (**a**) Schematic diagram of scenario 1: feedstock biomass is pretreated with dilute sulfuric acid; pretreated material is mixed with lime to raise pH and remove compounds inhibitory to downstream bioconversion; ethanol is purified by two-column distillation and molecular sieve adsorption; residual solids are removed from the distillation bottoms liquid and fed to a power plant boiler; distillation bottoms liquid is concentrated by evaporation with the resulting syrup also being fed to the boiler; remaining wastewater is treated onsite by anaerobic digestion then recycled to the process. (**b**) Schematic diagram of scenario 2: feedstock biomass is pretreated with AFEX and delivered directly to bioconversion with no detoxification required; after bioconversion, ethanol is purified using a single distillation column with IHOSR and molecular sieve adsorption; residual solids are removed from the distillation bottoms liquid and fed to a TC processing operation; distillation bottoms liquid is treated onsite anaerobic digestion and recycled to the process., AFEX, ammonia fiber expansion; IHOSR, intermediate via heat pump and optimal sidestream return; TC, thermochemical.

On-site cellulase production, costing 30 cents/gallon ethanol, is assumed for both scenarios based on our best-case estimate of what might be accomplished on a significant scale for a typical site and feedstock using current technology. We acknowledge that there is limited publicly available information on the cost of cellulase, and that a variety of factors affect this cost (**Supplementary Note**).

Figure 1 presents cost savings of potential R&D-driven improvements expressed as average percent reduction in processing costs evaluated with respect to scenarios 1 and 2. Process improvements associated with conversion of cellulosic biomass to sugars include the following: increasing cellulose hydrolysis yield (from 80% to 90%), halving cellulase loading (from 25 mg enzyme/g cellulose to 12.5 mg enzyme/g cellulose), eliminating pretreatment and incorporating consolidated bioprocessing such that enzyme production, hydrolysis and fermentation occur in a single process step[17]. Process

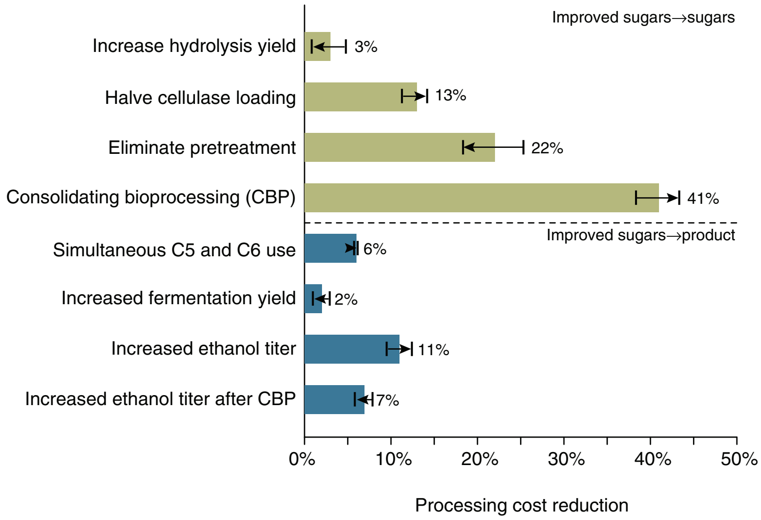

Figure 3 Reduction in processing costs for various technological advances. Values represent the average for the indicated advance (see main text) relative to two base-case configurations: first, scenario 1 at 2,205 dry tons feedstock/day; and second, scenario 2 at 5,000 dry tons feedstock/day. Error bars denote the range of processing cost reductions for scenario 1 and scenario 2, with the arrow pointing from scenario 1 to scenario 2. For scenario 1, ethanol titer is increased to 7 wt.%, the maximum value possible given the assumed yields and solids concentration used in pretreatment. For scenario 2, which entails less water used in pretreatment, the ethanol titer is increased to 10 wt.%.

improvements associated with conversion of sugars to ethanol include: simultaneous conversion of hexose and pentose sugars, increased fermentation yield (from 90% to 95% of theoretical yield) and increased ethanol titer (from 5% to 7% by weight for scenario 1 and 10 % by weight for scenario 2; see **Fig. 3** legend).The cost savings from improved conversion of cellulosic biomass to sugars are in general much larger than from improved conversion of sugars to ethanol.

Conclusions

The immediate factor impeding the emergence of an industry converting cellulosic biomass into liquid fuels on a large scale is the high cost of processing, rather than the cost or availability of feedstock (**Table 1**). Within the processing domain, potential R&D-driven improvements in converting biomass to sugars offer much larger cost savings in comparison to improvements in converting sugars to fuels (**Fig. 3**). The central issue to be addressed is thus improving technologies to overcome the recalcitrance of cellulosic biomass. This is true not only for ethanol but also for other biofuels produced by fermentation, as the cost of converting biomass to sugars must be lowered to have a cost advantage relative to sugar production from more easily-hydrolyzed raw materials, such as corn (**Fig. 1**). It may be noted that lowering the cost of sugar production from cellulosic biomass can be achieved by improved cellulose-hydrolyzing organisms or enzymes, improved processes for biomass pretreatment, new biomass feedstocks that are more easily processed or a combination of these.

Looking beyond industry emergence to large-scale application, the second central challenge is sustainable production of cellulosic biomass in very large amounts using a feasible amount of land. Attention thus far has focused almost entirely on crops and cropping systems that were chosen and developed for purposes other than energy production (food, feed or fiber). This likely will change as processing challenges are overcome. Achieving high land fuel yield is a key objective to both improve feedstock economics and minimize the ecological footprint of biofuel production. Future increases in biomass production per unit land and fuel production per unit biomass could together result in a roughly tenfold increase in land fuel yield compared with today, enabling scenarios in which biofuels play a large energy service supply role[10]. New crops and cropping systems will likely be developed that are conducive to coproduction of feedstock and feed in response to new demand for nonnutritive cellulosic biomass. Although it is reasonable to expect that environmentally advantageous biofuel production from cellulosic feedstocks can be achieved, realizing this objective will be fostered by rigorous evaluation and exploration of alternative production and management practices, crops and cropping systems responsive to local circumstances, and policies that reward environmentally desirable outcomes.

Biotechnological approaches—including systems biology, imaging and computational tools—are likely the most powerful approach available to address the dual challenges of biomass recalcitrance and large-scale sustainable production. By focusing the transformative power of biotech on these challenges, while considering sustainability in all its dimensions, we can reasonably hope to enable the 'second industrial revolution' that society now requires[18].

Note: Supplementary information is available on the Nature Biotechnology website.

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COMPETING INTERESTS STATEMENT
The authors declare competing financial interests: details accompany the full-text HTML version of the paper at http://www.nature.com/naturebiotechnology/.

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