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Survival of the Fittest: An Economic Perspective on the Production of Novel Biofuels

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Introduction

That the world is in need of renewable sources of energy has become a modern-day platitude. In the case of transportation fuels, drop-in biofuels have attracted increasing attention, while so-called "first generation biofuels" have continued to gain market access (here, first generation biofuels refer to ethanol and biodiesel from feedstocks that could be otherwise used for human consumption, while drop-in biofuels refer to those that can be blended with current fuels in any proportion and without modifying the existing infrastructure).

Drop-in (liquid) biofuels have, in general, various advantages: compatibility with the *status quo* (piping infrastructure, internal combustion engine, supply logistics, etc.), high-energy density, reduction in greenhouse gas emissions, and the possibility of providing energy security. The latter is especially important for countries that have agricultural resources but not enough oil resources to power their transport (including many developing countries that are unlikely to significantly benefit from electric vehicles in the foreseeable future due to grid infrastructure limitations). Drop-in biofuels have a distinct advantage in their high-energy density, since they can address markets that would be unavailable to other renewable energy solutions, in particular the market for jet fuel replacements.[1] As compelling as all these advantages might be, drop-in biofuels compete with fossil fuels almost exclusively on economic grounds, because fuels, like other energy products, are commodities with few differentiating features.[2] Even when the environmental benefits have been advertised, customers have shown little desire to pay a "green premium".[3]

In an attempt to develop the drop-in biofuel market, the research community that addresses biological routes for biomass conversion has proposed a variety of new candidate compounds based on a diverse array of metabolic pathways. These compounds may have the potential to replace fossil fuels with renewables.[4–8] Nevertheless; little attention has been given to the economic merits or demerits of these proposed novel fuels. The result is the proliferation of projects and even companies that aim at producing novel fuels via various metabolic pathways with little regard to their economic potential and ultimately their prospects for competing with fossil fuels on a large scale. If these factors are not considered, there is a slim chance that the long list of novel fuels will help in alleviating modern society's dependence on its oil resources. Considering them early on may focus the attention of the scientific community, save researchers valuable time, and spare society's money and resources.

Economic analysis of biofuel production

Even though there is much to gain from doing so, the factors that contribute to the cost of production are seldom

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analyzed when new compounds are proposed. There are many reasons for this: (1) the expertise of the researchers who develop novel biofuel pathways differs from that of the analysts who determine the cost of production, (2) when a new project is envisioned there is little information available to analyze all the costs, (3) the economics of production are determined by various factors, so that economic viability depends on the cooperation of many branches of science and engineering, and (4) many novel efforts are carried out in academia, where the aim is not to produce commercial products, and, therefore, economic factors are not considered, etc.

Even though there are clear hurdles for evaluating the economics of new compounds, we believe this is essential. Furthermore, even though production costs cannot be determined with any credible level of precision for most novel drop-in biofuels proposed due to lack of data, a final estimate is not needed for the analysis to be useful. Much can be learned from focusing on trends, cost drivers, and generalities, as we show in this article. We have used biofuels as an example of metabolic products of interest, although other compounds produced via industrial biotechnology can be similarly studied.

In the most general terms, the elements that contribute to the cost of production relate to: capital (facility-dependent), raw materials, utilities (steam, power, cooling water, etc.), labor, consumables (catalysts, membranes, etc.), transport, and waste treatment. From these, and for the case of biofuels produced through biochemical processes, capital and raw materials are usually the most significant, whereas consumables and labor are usually not substantial. We have ignored other operating costs that are independent of fuel choice, such as administrative, taxes, insurance, legal, etc. Utilities are usually less than10% of the cost of production, with largest contributions in processes that require large power usage, such as those needing centrifugation of large and dilute aqueous solutions. In general, it should be noted that heat is less expensive than power, and unless the process requires significant power use, utilities costs are manageable. It should also be mentioned that this discussion is limited to the economic consequences of a process, and that low energy costs relative to facilities or raw materials does not mean to imply low energy use or energetically-efficient processes. Transport costs can be included in the raw material cost, as will be discussed later in this article for the case of feedstock. Finally, waste treatment costs can also be significant, but are very process-dependent, and, thus, are hard to quantify for a generalized process. It must be noted that, even though not all costs are covered in depth in this discussion, a full analysis should include all of them, since customer decisions on fuel purchases can be swayed by cents per gallon.

From the perspective of microbially-derived biofuels, the parameters of significance to the cost of production are the yield, productivity, titer, and purity. The choice of feedstock has interesting implications on the economics of production and it is also briefly covered. We discuss each of them in turn.

The effect of yield

In this context, yield is the amount of product produced per unit of substrate consumed. The metabolic yield depends on the metabolic pathway used, and therefore it differs from the pathway-independent chemical yield (i.e., the amount of product that could be produced theoretically based on the elemental composition of the substrate(s) and product(s)). The yield differs from the conversion (or extent of reaction), which is the amount of the substrate that reacts or is consumed as a fraction of the initial amount of substrate present. For the purposes of the type of process economics we will discuss here, however, the yield and conversion can be combined in a quantity that we can call "overall yield", the total amount of product that leaves the process per unit of substrate that enters the process. Given the aforementioned definitions, the overall yield impacts the economics of production principally via the raw material cost. Because the raw material cost is expected to be the most significant contribution to the production cost of biofuels, the overall yield is very important.[9] Indeed, even in capital-intensive processes, such as production of lignocellulosic ethanol, the overall yield has been shown to be a main determinant of the minimum ethanol selling price, MESP.[10]

Although the overall yield depends on many factors that are hard to specify at the beginning of a research project (e.g., the success of the metabolic changes that can be introduced into a producing strain, the potential progress of media optimization campaigns, the quality of the feedstock to be used, among others), the maximum theoretical yield corresponds to the minimum production cost at a particular feedstock cost. This assumption corresponds to the case in which the capital required is either vanishingly small (see below), or can be "amortized" over an infinite number of product units. Furthermore, it requires one to assume that the transformation from raw material to product requires no energy inputs or labor, produces no waste to be treated, etc. All these assumptions are obviously unrealistic, but assuming a zero processing cost allows us to calculate the minimum production cost based only on raw material costs, which are inescapable.

As Table 1 shows, the minimum production cost derived from the theoretical yield varies for different biofuels and for different pathways. Two sugar prices are considered, the first is for sucrose in A molasses,[1] the second assumes 35 ¢/lb, as an arbitrary maximum for sugar price in the foreseeable future (noting that sugar prices reached ~30 ¢/lb in January and July of 2011[11]). The yields shown are pathway dependent, and were derived from the literature.[4–8,12,13] As can be seen in the table, fermentative or otherwise less reduced products (e.g., ethanol, isobutyl alcohol) have higher theoretical yields, and, therefore, lower raw material costs. On the other hand, highly reduced products with low-theoretical yields (e.g., squalene) have higher raw material costs.

It may be argued that chemically reduced fuels might be more expensive, but they are also more energy dense. Therefore, it might be concluded, evaluating the cost on a volume basis is not a fair assessment, so any comparison should be done on an energy basis. In fact, the most adequate comparison would be an analysis on the distance traveled per unit of biofuel consumed (e.g., miles per gallon - MPG). These compounds will be used for transportation, and the combustion properties vary across the various biofuels, so that

Table 1. The Raw Material Cost Contribution to the Production of Various Types of Biofuels Biochemical Pathways to Fuels is Indicated

Biofuel	Pathway	Density (kg/L)	Mass Yield (g/g)	Volume Yield (gal/MT)	RM cost $/gal (15.5 c/lb)	RM cost $/gal (35 c/lb)
Ethanol	Fermentative	0.79	0.51	171	$2.00	$4.51
Butanol	Fermentative	0.81	0.41	134	$2.55	$5.76
Isopropanol	Fermentative	0.786	0.33	111	$3.07	$6.94
Isobutanol	Non-fermentative	0.81	0.41	134	$2.55	$5.76
3-methyl-1-butanol	Non-fermentative	0.81	0.33	108	$3.17	$7.15
Farnesene	MVA	0.84	0.25	79	$4.34	$9.79
Farnesene	DXP	0.84	0.29	91	$3.74	$8.44
Ethyl hexadecanoate	Fatty acid	0.86	0.35	108	$3.17	$7.16
Pentadecane	Fatty acid	0.77	0.29	100	$3.43	$7.74
Squalene	MVA	0.86	0.25	77	$4.44	$10.03
Squalene	DXP	0.86	0.29	89	$3.83	$8.64
Alpha-pinene	DXP	0.85	0.32	99	$3.43	$7.74
Isopentenol	DXP	0.839	0.376	118	$2.88	$6.50

Abbreviations: MVA mevalonic acid pathway; DXP deoxyxylulose-5-phosphate pathway; RM raw material; MT metric ton

energy density is still not the most relevant metric for comparison. Because extensive engine and field tests have not been conducted on the different fuels, the energy density is used here as a proxy for comparison. As Table 2 suggests, the increase in energy density of drop-in biofuels does not entirely compensate for the reduction in metabolic yield, and it is unlikely that this trend will be reversed when comparing them on engine test data. For instance, ethanol fuel additives have proven beneficial, as the compound boosts octane rating and thus improves engine performance.

The importance of yield suggests that any drop-in biofuel that will be commercialized must be produced at near theoretical maximum values. Optimizing yield requires campaigns of metabolic engineering to ensure that the sugar substrate is converted to the compound of interest and not "wasted" in producing biomass, energy, or metabolic byproducts. The ability to engineer a system to maximize the yield is therefore limited by the cell's requirement to meet its energy and reducing equivalent needs.[4] There is, therefore, an intrinsic advantage in producing biofuels from pathways that (a) have a high theoretical maximum yield, (b) are redox balanced, and (c) provide adequate levels of energy. Anaerobic processes have lower cell mass yields and do not waste sugars to recycle unbalanced reducing equivalents as is the case in many aerobic biofuels production pathways.

The effect of productivity

Productivity can be defined for the purposes of this discussion as the amount of product biosynthesized per unit volume of fermentation per unit time. Other productivity metrics that are of interest to the economics of production could be proposed, but this one is easy to measure and has been reported for laboratory experiments for various biofuels. It must be noted that productivity (in g/L•h or a similar unit) is time-dependent, thus, the quantity we refer to in this discussion is the average productivity.

Productivity is related to the capital cost of fermentation, as faster reactions would need lower residence times, and, thus, smaller fermentors. This implies that the capital cost of the facility will scale inversely with productivity, and the cost of production will follow a similar trend (*ceteris paribus*).

Table 3 shows productivity data for various biofuels.[7,8,12,13] Although the majority of the data was collected in laboratory conditions, which have not been optimized and are very different from industrial conditions, we have used it to provide a rough estimate of the current cost of

Table 2. Raw Material Costs Contributions for the Production of Various Biofuels Based on the Energy Density of the Biofuel

Biofuel	Pathway	$-\Delta H_C$ (MJ/kg)[a]	RM cost $/GJ (15.5 c/lb)	RM cost $/GJ (35 c/lb)
Ethanol	Fermentative	29.7	$22.51	$50.84
Butanol	Fermentative	36.1	$23.04	$52.02
Isopropanol	Fermentative	30.45	$33.94	$76.63
Isobutanol	Non-fermentative	35.9	$23.17	$52.31
3-methyl-1-butanol	Non-fermentative	37.7	$27.41	$61.89
Farnesene	MVA	47	$29.02	$65.53
Farnesene	DXP	47	$25.02	$56.49
Ethyl hexadecanoate	Fatty acid	39.4	$24.73	$55.84
Pentadecane	Fatty acid	47	$25.02	$56.49
Squalene	MVA	47	$29.02	$65.53
Squalene	DXP	47	$25.02	$56.49
Alpha-pinene	DXP	45.5	$23.42	$52.88
Isopentenol	DXP	37.3	$24.31	$54.90

[a]Heat of combustion

Table 3. The Influence of Productivity on the Required Fermentation Volume and Cost for Production of 20 Million Gallons Per Year of Various Biofuels

Biofuel	Titer (g/L)	RT[a] (hr)	Productivity[b] (g/L/hr)	Number of 900 m^3 reactors (approx.)[c]	Cost (approx.)[d]	Amortized over 10 yr ($/gal)
Ethanol[e]	94.8	10	9.48	3	$2,250,000	$0.01
Isopropanol	143	240	0.60	53	$39,750,000	$0.20
Butanol	30	168	0.18	182	$136,500,000	$0.68
Isobutanol	22	110	0.2	163	$122,250,000	$0.61
Farnesol	0.135	48	2.81E-03	12,677	$9,507,750,000	$47.54
FAEE	0.43	72	5.97E-03	5,923	$4,442,250,000	$22.21
Fatty Alcohols	0.06	72	8.33E-04	40,036	$30,027,000,000	$150.14
Alkanes	0.3	40	7.50E-03	4,127	$3,095,250,000	$15.48
Farnesene	100	144	0.69	49	$36,750,000	$0.18
Butanol	113.3	326	0.35	94	$70,500,000	$0.35

[a]Residence time.
[b]average productivity.
[c]for a 20 million gal/y facility.
[d]equipment purchase cost only.
[e]industrial conditions, sugarcane process with cell recycle.[12]

fermentation for each product. The methodology can be repeated as new data is gathered. The table assumes a 20 million gallon per year facility for all cases, and a fermentor size of 900 m^3 each. This size is relatively small for anaerobic fermentations (and, thus, unnecessarily expensive), but at the limit of what could be achieved for aerobic fermentations. A single reactor design for all fermentations is a very crude assumption, as fermentors are usually custom-designed and matched to the specific requirements of the process at hand. However, the assumption allows us to comparatively evaluate different fuels and benchmark them to ethanol, the only biofuel on the list that is commercially produced in large quantities today.

The table shows that the amortized cost of the fermentors is almost insignificant for ethanol and would be prohibitively expensive for the most novel biofuels. Even for butanol and isobutyl alcohol, which have been proposed as substitutes for ethanol in the relatively short term, the estimated fermentor cost (based on laboratory-scale data) is several times higher than for ethanol. One advantage of ethanol has been that it is naturally produced by yeast with high yield (close to theoretical values) and high tolerance to the biofuel. The high productivity is achieved by a high-cell density fermentation allowed by biocatalyst recycle. A similar tactic could and should be used when producing other compounds in industrial scales, although biocatalyst reuse requires that cells remain active, and, thus, toxicity might become an issue for some compounds (e.g., butanol). Increasing the concentration of the pathway enzymes can also boost production rates, but there is a practical limit on this strategy before the health of the cell is compromised. Lastly, engineering enzymes with faster reaction rates could be used to improve productivity, but this effort is, in general, infinitely harder compared to the preceding two.

At the most fundamental level, productivity is limited by the rate at which pathways operate. Deconstructive pathways, in which complex molecules are broken down to simpler molecules, have an advantage in this regard compared to constructive pathways, in which simpler substrates or pathway intermediates are used to build larger and more complex molecules. Ethanol belongs to the former, whereas hydrocarbon molecules to the latter. Biofuel-producing pathways should thus aim to have few constructive steps, especially if those involve complex transition states with slow kinetics.

The effect of titer, purity, and feedstock

Titer is the concentration of the desired product achieved in fermentation, whereas purity is the concentration of the desired product as a percentage of the various fermentation products. Purity is usually not a focus when discussing biofuels, first, because its effect is included in the effect of yield (higher yield results in purer products), and second, because combustion does not require a particularly pure product, as long as the product (or product mixture) conforms to certain specifications. Purity, in other words, is not a parameter that can make or break the economics of production in the case of biofuels. Indeed, the fossil fuels we use (gasoline, jet fuel, diesel) are mixtures of hydrocarbons, rather than pure compounds. Therefore, we will not discuss purity any further.

Titer is important, on the other hand, because a relatively concentrated product makes downstream processing easier and minimizes the loss of product (which ultimately lowers overall yield). Titer may be limited by the achievable or practical substrate concentration and/or byproduct toxicity. A process with low titer, i.e., a dilute process, must employ more unit operations and more energy to separate the product of interest from the rest of the process.[8] Additionally, a dilute process requires larger equipment per unit of product produced.

More expensive facilities can also result from complexities arising from feedstock choices. For example, lignocellulosic ethanol plants have more complex upstream processes than corn ethanol plants. The former requires several elaborate steps to convert the polysaccharide fibers in the feedstock to fermentable sugars, whereas the latter requires simpler steps. In addition, lignocellulosic processes result in a mixture of sugars and inhibitors that are harder to ferment compared to the comparatively pure stream of sugars that result from the starch- or sucrose-based processes. Lignocellulosic biomass is generally less expensive, on a weight basis, than other substrates for fermentation (starch, sucrose, glucose, etc.), but by and large the lower raw material cost has hitherto failed to compensate for other shortcomings of the

Table 4. The Effect of Scale and Type of Feedstock on the Capital Cost (Expressed as $ Per Annual Gallon) for Various Processes

Feedstock / Process	Product(s)	Capital (US$M)	Annual Capacity (1000gal)[a]	$/annual gal	Company/ Location
Corn/milo, fermentation	Ethanol, DGS	$132	60,000	$2.20	Aemetis, Modesto[15]
Corn stover/cobs, fermentation	Ethanol	$250	25,000	$10.00	POET-DSM, Emmetsburg[16]
Sugarcane, fermentation	Ethanol, power	$240	70,000	$3.43	Typical value, Brazil[b17]
Agri-residues, waste, gasification-fermentation	Ethanol, power	$130	8,000	$16.25	Ineos Bio, Vero Beach[18]
Agri-residues, fermentation	Ethanol	$77	1,400	$55.00	Verenium, Jennings[19]
Agri-residues, fermentation	Ethanol	$25	1,980	$12.63	Praj, Maharashtra (India)[c20]
Renewable diesel, fermentation	Farnesane	$60	13,210	$4.54	Amyris, Brotas (Brazil)[d21]
Corn, fermentation	Isobutanol	$38	18,000	$2.09	Gevo, Luverne[e]
Conventional refinery	Petrol, diesel, etc.	$5,000	3,024,000	$1.65	Typical value, Survey
Forest residues, catalytic cracking	Biocrude (for diesel, petrol, etc.)	$213	13,000	$16.38	KiOR, Columbus[22–24]
Gas-to-liquids (GTL)	Petrol, diesel, etc.	$16,000	1,451,520	$11.02	Sasol, Westlake[25]

[a]In most cases, capacity is projected, not actual.
[b]assumes no sugar production, 80 L/MT sugarcane and 2 BRL/USD.
[c]assumes a yield of 60 gal/MT (dry).
[d]Capex estimate adapted based on the model published in Ref. 1 and from SEC filings.
[e]Capex includes brownfield plant purchase and retrofit.

biochemical processes that use this type of feedstock (e.g., lower yields, higher process complexity, lower productivity, etc.). Therefore, that inexpensive feedstocks in the form of lignocellulosic biomass will overturn many of these economic challenges of biofuels is a claim that should be considered on a case-by-case basis.

The type of feedstock also imposes a limit on the scale of the facility. The feedstock must be transported to the facility, and low-density feedstocks, like lignocellulosic biomass, must be sourced from farther afield than higher-density feedstocks for a particular scale. On the other hand, economies of scale in the plant commonly exist such that larger plants cost less per unit product than smaller plants. The optimal scale can therefore be chosen such that the diseconomies of scale in feedstock costs balance out the economies of scale in facility costs.[2,14]

The effect of scale and the choice of feedstock can be seen from Table 4. The table focuses on biochemical processes for production of biofuels, with conventional and thermochemical processes included for comparison. It must be noted that, with the exception of established technologies, the numbers in Table 4 are projections, and therefore the values for novel biofuels are unlikely to account for lower than expected yields, productivities, and titers. However, it is clear from the data that technologies based on lignocellulosic biomass are significantly costlier per annual gallon than those based on denser and easily processed feedstocks, and that larger facilities are less expensive per annual gallon than smaller facilities. Remarkably, out of the technologies covered, conventional refineries are the least expensive on an annual gallon basis, with impressive economies of scale achieved due to the readily transportable and very dense feedstock (crude oil).

Combining chemical and biological synthesis in the production of novel biofuels

The arguments and trends presented in the preceding discussion offer us a new perspective in evaluating the prospects of novel biofuel routes, and allow generalizing these trends to assess more complex production routes. Let us look at one example of this analysis. We learned that fermentation is well suited in the production of certain biofuels, but not others. In particular, it seems adept at synthesizing relatively simple and somewhat oxidized products through deconstructive pathways and less so at synthesizing complex and reduced compounds through constructive pathways. Biological synthesis is particularly impressive at utilizing a complex mixture of substrates (the most obvious example is lignocellulosic hydrolysate, but even sugarcane juice is replete of impurities) and selectively converting compounds in this mixture into one or more products of interest at relatively high yield. The high selectivity and yield are generally offset by relatively low productivity and titer. Chemical synthesis, on the other hand, is usually not as selective, but allows the use of high temperatures and pressures that speed up reactions and increase volumetric productivity. Furthermore, unlike biocatalysts, chemical catalysts usually do not become deactivated by high substrate or product concentrations, as long as these are reasonably pure. The production of novel biofuels might thus occur in two steps: (1) a clean intermediate stream can be synthesized through biological deconstructive pathways, and (2) the intermediate stream can be used as a substrate for chemical synthesis in a constructive fashion. For example, the products of the *Clostridial* ABE fermentation can be readily extracted and recombined to produce fuel precursor molecules.[26] Here acetone and n-butanol can be produced at near theoretical yields (but at low concentrations), selectively extracted from the aqueous fermentation broth and reacted at high yields to form gasoline, jet and diesel blendstocks. Companies like LanzaTech, Gevo, and Byogy Renewables are developing routes to produce kerosene-type jet fuels from fermentation-derived alcohols (the so-called alcohol-to-jet route, ATJ).[27]

A current limitation of the ATJ route is that, after accounting for the reaction yield in the chemical transformation, the end product may sell for less than the intermediate, so it might be more profitable to sell the intermediate and not the end product. For example, if 3.5 molecules of ethanol are needed per molecule of jet fuel, then $\sim$1.65 volumes of ethanol are needed to produce a volume of jet fuel. This is the theoretical minimum volume of ethanol needed assuming an average jet fuel composition of C_7H_{17}, and ignores the extra hydrogen needed to eliminate the oxygen in the alcohol. The ethanol price at the end of August 2013, according to the CME Group, was \$2.50/gal[28], placing the minimum jet fuel production cost via ATJ at \$4.12/gal, or \$1.09/L. This is comparable with the minimum cost of production of other drop-in biofuels in Table 1, with the advantage that it can be produced at high productivity: using the same calculation as in Table 3, an alcohol-to-hydrocarbon reactor[29] amortized over 10 years would have an estimated cost of \$0.06/gal, placing the total of ethanol fermentation plus hydrocarbon synthesis equipment at \$0.07/gal. However, according to the EIA, the jet fuel price in August 2013 was ~ \$3/gal, or \$0.8/L.[30] In other words, the jet fuel revenue would not be, currently, enough to cover the opportunity cost of the ethanol intermediate, even operating at maximum theoretical yields and ignoring all other costs (including hydrogen).

An important consideration is that the forces that influence the renewable alcohol and fossil fuel markets are different. As fossil fuels become expensive and new technologies competitive, the ATJ and similar chemical-biological "hybrid" processes could become profitable. Short-chain alcohols will likely be adopted on a wide scale fastest: the ethanol market is relatively small but quickly growing at a projected annual rate of ~14.2% for the next 4–5 years[31]. These, however, cannot serve as drop-in biofuels in most of the world, and will not be adopted in aviation and for other long-haul needs. Combining comparatively high yields and productivities, hybrid processes may be promising routes for providing renewable, fungible biofuels at acceptable cost. One should not be forced to choose between biological and chemical synthesis, but instead consider combining them to exploit the best qualities of each route.

Conclusion

The main argument presented in this discussion is that the economics of production for new biofuels should and can be considered early in the R&D process. We offer a framework that can be applied to other biofuel production processes, specifically, that parameters such as the yield, productivity, titer, and the choice of feedstock, can quickly inform on the merits and potential challenges of a production process. It requires little data about the process and provides valuable information with minimal effort. It is similar in nature to other methods that have been proposed,[32,33] centering on fermentation routes and those where cost of production plays a fundamental role in the viability of the process, such as for bulk chemicals and commodities. The framework can also highlight areas in most need of improvement and suggest probable bottlenecks before much time is wasted. We used this set of principles to assess the potential of hybrid chemical-biological routes for production of drop-in biofuels, and expect it to be useful in informing the R&D community on the economic prospects of other novel biofuel production technologies.

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