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Combining Environmental and Economic Performance for Bioprocess Optimization

Opinion

Biochemical production faces economic and environmental challenges that need to be overcome to enable a viable and sustainable bioeconomy. We propose an assessment framework that consistently combines environmental and economic indicators to support optimized biochemical production at early development stages. We define internally consistent system boundaries and a comprehensive set of quantitative indicators from life cycle assessment (LCA) and techno-economic assessment (TEA) to combine environmental and economic performance in a single score. Our framework enables the identification of trade-offs across environmental and economic aspects over the entire biochemical life cycle. This approach provides input for the optimization of future biochemicals in terms of overall sustainability, to overcome prevailing obstacles in the development of biochemical production processes.

Global Demand for Chemicals Requires Environmentally and Economically Sustainable Alternatives

The doubling of biochemical production between 2011 and 2018 [1] is an important contributor to reducing dependency on fossil resources and related environmental impacts and to supporting a circular economy [2]. This trend is predicted to continue based on growing demand for biobased materials across sectors including packaging, automotive, building, and consumer goods (12–42% growth by 2021 compared with 2011) [1]. Increased scale-up potential and knowhow in the manipulation of cell factories and thermochemical technologies for selective and efficient production of target molecules has led to significant R&D (see Glossary) efforts to commercialize biochemicals [3,4].

Despite several reported environmental advantages of biochemicals, not all biochemicals are consistently more sustainable than functionally equivalent petrochemicals [5,6]. To optimize the sustainability performance of biochemicals, both environmentally and economically, it is important to understand where along a biochemical’s life cycle relevant hotspots (i.e., major environmental problems or costs) occur and how changes in life cycle inputs (resources used) and outputs (emissions into the environment) can reduce such hotspots [7–9].

Currently, biochemicals represent about 2% of the global commodity chemicals market, with projections exceeding 20% by 2025 [10]. Reaching this level of market contribution, however, requires addressing of current economic sustainability challenges. For example, the lack of economic competitiveness of biochemicals renders their production vulnerable to fluctuations in the supply and demand of fossil-based chemicals and biofeedstocks [11]. Along with relatively complex supply chain dynamics, this currently hampers rapid growth of the biochemicals market [8,12,13].
From an environmental perspective, there are additional challenges for biochemical production, since biochemicals are not necessarily sustainable just because they are produced from renewable feedstocks [5,6]. For example, intensive use of synthetic fertilizers in crop-based biofeedstocks contributes to increased eutrophication, rising demand for land leads to direct and indirect changes in land use, and the impact of water use increases with extended and intensified farming. Hence, claiming environmental sustainability of biochemicals based on reduced contribution to global warming (from reduced greenhouse gas emissions, which is often the main contributor to the environmental impacts of fossil-based chemicals) can be misleading if other environmental impacts are neglected, which are mainly related to feedstock production and energy-intensive pretreatment and biorefinery processes [5,6]. To achieve an overall sustainable performance for biochemicals, both economic viability and environmental sustainability challenges need to be addressed [14–19].

Today, building block biochemicals are largely produced from agricultural crops (first-generation feedstock [20]), mostly with high technological readiness levels (TRLs) of 8 (first-of-a-kind commercial system) or 9 (full commercial application) [21] (Table 1). Production capacities for building block biochemicals and derived polymers continue to grow at approximately the same rate as production capacity for building block petrochemicals, that is around 3–4% annually [25]. Biochemical production from lignocellulose or wood (second-generation feedstocks [20]) has not yet reached high TRLs due to relatively low fermentable sugar content, high sugar conversion costs [26], and low technical process maturity [20]. The complexity of feedstock supply chains currently hampers the economic viability of biochemicals from second-generation feedstocks [12]. Due to these challenges, new feedstock sources with low TRLs of 2–3 are being explored; these include engineered crops, algae, and urban residues like household waste (third- and fourth-generation feedstocks [6,19]). Among these emerging feedstocks, brown algae receive significant attention due to the absence of lignin in their biomass, thus avoiding the need for lignin removal [3,27]. Lignin removal is costly because of the recalcitrance of lignocellulosic cellulose and toxic effects on microbial properties [28]. As promising feedstocks and associated preprocessing technologies emerge, it is critical to optimize these production systems in terms of both economic and environmental sustainability to achieve market competitiveness.

In typical industrial biotechnology R&D paradigms, several decisions are made when designing a cell factory, which then often face enormous economic and environmental challenges on scale-up to market level. For instance, during strain optimization, strains are mainly selected based on yield, titer, and productivity. However, the presence of specific byproducts may lead to higher associated downstream processing costs. Similarly, for proper upstream conversion or downstream separation of impurities, extensive use of chemicals or utilities may result in increased environmental impacts. To consider such scale-up problems, the environmental and economic performance of biochemicals production should be evaluated early in the technology development process and ideally be combined to identify possible trade-offs [29]. To evaluate both environmental and economic sustainability performance, different assessment methodologies and stakeholder perspectives need to be included in an iterative approach. In response to this need, we propose the systematic combination of environmental life cycle impacts and techno-economic performance in a consistent decision support framework to optimize biochemical production processes.

Performance Assessment of Biochemicals: Context and Fundamentals
Assessing the economic viability of future technologies is an integral part of product development in biotechnology, mainly due to substantial development costs in turning ideas into commercialized products. To assess technical and economic feasibility, TEA (Box 1) is a widely used tool that

Glossary
Biofeedstock: an organic substrate that can be converted into biochemical products. Biofeedstocks are divided into generations depending on the state of development of methods to use the biomass for biochemical production. Agricultural crops are defined as first-generation biofeedstock, lignocellulose or wood as second generation, and engineered crops, algae, and organic (municipal and/or agricultural) wastes as either third or fourth generation (a general definition of third- and fourth-generation biofeedstocks is currently not available).

Building block biochemicals: molecules that build the foundation of various secondary chemicals and intermediates derived for different applications and uses.

Functional unit: a quantitative description of the function or service of any given product system for which an assessment is performed. An example of a functional unit is the utilization of 1 kg of lactic acid, with 99.9% purity, for household product packaging application in the USA.

Hotspots: in assessment results, impacts that stand out compared with other results. Identification of hotspots in TEA and/or LCA shows where to focus future process optimization with respect to the chosen indicators for the given product.

Life cycle: here, the different stages a biochemical goes through during its lifetime. A full life cycle of biochemical production (e.g., derived via microbial fermentation) includes the following stages: (i) cultivation and harvesting; (ii) biomass pretreatment; (iii) fermentation and purification; (iv) product making (application dependent; e.g., forming, molding); (v) product use; and (vi) waste handling.

Research and development (R&D): refers to activities initiated to develop new products, services, or product systems or to further improve already available products, services, or product systems.

Technological readiness level (TRL): a tool developed by the National Aeronautics and Space Administration (NASA) to consistently and uniformly estimate the maturity of technologies. The scale ranges from TRL 1, which defines the lowest level of technological readiness, to TRL 9, which is the highest level of technological readiness, the technology in its final form.
helps companies define internal optimization targets to reach market sustainability. To assess the environmental sustainability of biochemicals as an emerging field, product LCA (Box 1) is gaining increasing attention in support of the global sustainable development agenda and a viable bioeconomy [6]. Technological improvements may at times lead to reduced environmental impacts, while in other cases economic benefits may come at the expense of increased environmental burden. Only when both TEA and LCA are combined in a consistent framework, related trade-offs can be addressed to optimize biochemical production. In support of a combined framework, we discuss the strengths and limitations of applying TEA and LCA to biochemicals separately and in combination.

Assessing the Economic Sustainability of Biochemicals
To assess the technical feasibility and economic sustainability of biochemicals, TEA is widely used, with numerous published studies [9]. Some examples are provided in Table 2. Existing TEA studies mostly focus on first- and second-generation feedstocks and specific process configurations in support of direct comparisons of different products and processes, while emerging feedstocks are rarely assessed to date. The National Renewable Energy Laboratory (NREL) has been one of the key contributors to this research field and has set the standard for high-quality assessments [63].

Assessing the Environmental Sustainability of Biochemicals
The environmental sustainability of biochemicals is becoming increasingly important in the development of biochemicals, with some studies applying LCA [5,6]. Examples are provided in Table 2. There are surprisingly few LCA studies available assessing commodity chemicals, such as lactic acid, succinic acid, and 1,3-propanediol. Moreover, many relevant life cycle stages, such as product application (use stage of the final product) and end-of-life handling (e.g., recycling, waste disposal), are often not assessed. However, when life cycle stages are neglected, the environmental sustainability claims of biochemicals may quickly become questionable [6].

Parallel Economic and Environmental Sustainability Assessment
In addition to performing TEA and LCA separately for biochemicals, results from both tools can be combined to evaluate the environmental and economic sustainability for optimization of individual processes [49] or to assess different process designs [51,53]. Some examples are given in Table 2. Combining TEA and LCA requires a broader perspective than process optimization. This includes covering the entire biochemical life cycle from feedstock selection to waste handling and considering the broad range of environmental impacts and economic indicators, including those related to process scale-up.

With growing demand for sustainable biochemicals, industrial biotechnology could immensely benefit from early-stage assessments that guide the development of both economically and environmentally viable processes. This approach helps to identify trade-offs that a separate application of TEA and LCA would not be able to reveal, which would lead to unnecessary environmental or economic impacts that could be avoided from the earliest stages of process development. However, a quantitative method that consistently combines a comprehensive set of indicators from both TEA and LCA and that translates these indicators into a combined score is currently missing. In response, we propose such a combined framework and discuss its application to the early stages of biochemical production process R&D.

Consistent Combination of Economic and Environmental Indicators
Outlining a Combined Assessment Framework
The starting point for consistent combination of TEA and LCA to assess biochemicals at early development stages is to define a common functional unit (e.g., 1 kg of a target biochemical

Trade-offs: the increase in performance of one indicator and simultaneous decrease in performance of another indicator. Trade-offs occur, for example, when economic performance is improved due to a change in product composition or production system, which negatively affects environmental performance results, or vice versa. This is also referred to as ‘burden shifting’ from one aspect (that improves) to another (that gets worse).

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produced for a specific plastic product application) and derive common assessment boundaries for the technological system (e.g., aligning the assessed system by including incineration of unfermented biosolids from the fermentation for energy production [7]). Chemical process modeling in the TEA component creates the required inventory data for the LCA, which aligns TEA and LCA in terms of data compatibility for all assessed processes. To finally align TEA cost outputs with environmental impact results, LCA impact indicators (e.g., climate change, eutrophication, land use [6]) are translated into monetarized damage using monetary valuation. This facilitates a consistent aggregation with TEA results into a single score reflecting total costs per functional unit. All proposed alignment aspects are illustrated in Figure 1.

| Biobased building block chemical | TRL (estimated if not found in literature) | Feedstock for biobased products | Global production volume/capacity (kt/year) from various sources, from 2015 to 2019 |
|---------------------------------|------------------------------------------|---------------------------------|-------------------------------------------------|
| 1,3-Propanediol (1,3-PDO)       | 8–9 [21]                                 | Corn glucose, sugars and glycerol [21] | -130 (estimated worldwide production capacity) [1] |
|                                 |                                          |                                 | 128 [21]                                           |
| 1,4-Butanediol (1,4-BDO)        | 8–9 [21]                                 | C5 and C6 sugars [21]            | -60 (estimated worldwide production capacity) [1] |
|                                 |                                          |                                 | 3 [21]                                              |
| 1,5-Pentamethylene diamine (DMS), cadaverine | 8–9 | Decarboxylation product of the amino acid lysine [22] | -50 (estimated worldwide production capacity) [1] |
| 11-Aminoundecanoic acid (11-AA) | 6–7                                      | Castor oil [23]                 | -30 (estimated worldwide production capacity) [1] |
| 2,5-Furandicarboxylic acid (2,5-FDCA) | 5–6 [21]                              | Starch crops, 5-hydroxymethylfurfural [21] | -30 (estimated worldwide production capacity) [1] |
|                                 |                                          |                                 | 0.045 [21]                                         |
| Adipic acid (AA)                | 4–5 [21]                                 | Sugars [21]                     | -10 (estimated worldwide production capacity) [1] |
|                                 |                                          |                                 | 0.001 [21]                                         |
| Dodecanedioic acid (DDDA)       | 4–5 [21]                                 | Plant oil feedstock [24]        | -10 (estimated worldwide production capacity) [1] |
| D-Lactic acid (D-LA)           | 8–9 [21]                                 | Corn, cassava, sugar cane or beets, C5 and C6 sugars [21] | -20 (estimated worldwide production capacity) [1] |
| L-Lactic acid (L-LA)           | 8–9 [21]                                 | Corn, cassava, sugar cane or beets, C5 and C6 sugars [21] | -700 (estimated worldwide production capacity) [1] |
| Lactide                         | 8–9 [21]                                 | Corn, cassava, sugar cane or beets [21] | -50 (estimated worldwide production capacity) [1] |
| Epichlorohydrin (ECH)           | 8–9 [21]                                 | Glycerol [25]                   | -490 (estimated worldwide production capacity) [1] |
| Ethylene                        | 8–9 [21]                                 | Glucose [1], sugar cane, sweet sorghum, corn [21] | -200 (estimated worldwide production capacity) [1] |
|                                 |                                          |                                 | 200 [21]                                           |
| Isosorbide                      | 7–8 [21]                                 | Glucose [1]                     | -20 (estimated worldwide production capacity) [1] |
| Monoethylene glycol (MEG)      | 7–8                                      | Sugarcane and second-generation sugars [21] | -310 (estimated worldwide production capacity) [1] |
| Monopropylene glycol (MPG)     | 7–8                                      | Glycerol [25]                   | -130 (estimated worldwide production capacity) [1] |
| Sebacic acid                    | 8–9                                      | Castor oil [1]                  | -150 (estimated worldwide production capacity) [1] |
| Succinic acid (SA)              | 8–9 [21]                                 | C5 and C6 sugars [21]           | -70 (estimated worldwide production capacity) [1] |
|                                 |                                          |                                 | 38 [21]                                            |
While the monetized results for each TEA and LCA indicator help to identify the predominantly contributing processes (hotspots), combining all results into a single score helps to identify trade-offs across environmental and economic indicators. Both require consideration of a comprehensive set of TEA and LCA indicators, including, for example, impacts from indirect land-use change relevant for different feedstocks [7,64]. Our overall set of proposed indicators is presented in Figure 2.

Impact monetization has been used before in LCA studies [65–67] but has not yet been applied to arrive at a single score to combine TEA and LCA results for biochemicals. Results for resource-related LCA indicators (e.g., mineral and fossil resource scarcity) and for all TEA indicators are already expressed in monetary values. Human health damage in LCA is commonly expressed as disability-adjusted life years (DALYs), which can be translated into cost equivalents using, for example, a monetary value of US$100 000/DALY [68]. By analogy, ecosystem quality damage in LCA is expressed as lost species-years, which can be translated into cost equivalents using, for example, a value of US$65 000 per lost species-year [66]. However, there are also challenges related to the accurate and objective monetization of human health and ecosystem damage. For example, as demonstrated for damage from greenhouse gas emissions, there are substantial differences in monetary values for human health damage mainly due to differences in the considered macro- and microeconomic factors, such as decreased working capacity and malnutrition [68]. Additional challenges are related to subjective value choices in the monetization [69], which involve moral questions that affect any framework adopting monetized values for human or environmental health. The uncertainty of monetary values is therefore high, which needs to be reflected when interpreting monetized damage results along with reporting the basis for the monetization, such as willingness to pay [66] or the value of statistical life [70]. Hence, refined monetary values should be applied as soon as they become available for a given decision context and always be transparently reported. This can easily be accommodated, since our framework is modular, which would also help to identify values that would render a proposed technology economically competitive in a specific decision context.

**Application of the Combined Assessment Framework**

We applied our combined TEA and LCA assessment framework in an illustrative case study to evaluate trade-offs between different feedstocks and production systems for the ‘production Box 1. TEA and LCA to Optimize Biochemical Production

**TEA**

TEA is a methodology that builds on the information derived from thermodynamic and material data for process development and technical optimization. Data inputs are usually processed via process systems engineering (PSE) tools such as Aspen© and SuperPro, which can estimate the economic viability of conceptual biochemical production processes. TEA provides insights into the technological impacts and costs of various sections in the overall production process by assigning monetary values to all of the materials, energy, and other consumables needed to run a production facility. Applying TEA has helped stakeholders to understand the long-term economic impacts of technologies at various commercialization levels [75–77].

**LCA**

LCA is a standardized method that involves cradle-to-grave (for biochemicals, from biomass extraction to product manufacturing, use stage, and end-of-life handling such as waste treatment) or cradle-to-gate (excluding use stage and waste handling) analyses of production systems. LCA provides comprehensive inventories [in the life cycle inventory (LCI) analysis phase] and related impact evaluations [in the life cycle impact assessment (LCIA) phase] of all upstream and downstream energy and other resource inputs and multiple environmental emission outputs [78,79]. LCA studies can be costly and time consuming. However, the efficiency of conducting LCA can be increased by using TEA as a tool to generate the required process data on LCI inputs and outputs along the product life cycle [7].
### Table 2. TEA and LCA Studies Applied to Evaluate Processes in the Production of Biochemicals

| TEA and/or LCA | Chemical or fuel type | Feedstock | Assessed environmental impact category<sup>a</sup> | Application/intention of study and stage of development | Early stage | Refs |
|---------------|----------------------|-----------|---------------------------------------------------|--------------------------------------------------------|-------------|------|
| TEA           | Biodiesel            | Mixed wood and corn stover | – | Process design | – | [30] |
|               | Biodiesel and co-production of SA | Glycerine | – | Process design | – | [31] |
|               | Ethanol              | Softwood  | – | Process assessment | – | [32] |
|               | Drop-in biofuels     | Jatropha   | – | Process assessment | – | [33] |
|               | Ethanol, PHB         | Sugarcane  | – | Process assessment | – | [34] |
|               | Ethanol, LA, methanol| Lignocellulosic residues | – | Process assessment | – | [35] |
|               | Carboxylic acids     | Sawdust    | – | Process assessment | – | [36] |
| LCA           | SA                   | Lignocellulosic residues | GHG, CED | Process assessment | – | [37] |
|               | SA                   | Corn       | CC, EU, ET, HT, OD, MD, and many more | Process assessment | – | [38] |
|               | LA                   | Corn       | GHG, CED | Process assessment | – | [39] |
|               | LA                   | Lignocellulosic residues | GHG, CED, PM, AC, ET, EU, HT, LU, OD | Process assessment | – | [40] |
|               | 1,3-PDO              | Corn       | GHG, CED, EU, HT, ET, AC | Process assessment | – | [41] |
|               | 1,4-BDO              | Corn       | GHG, CED | Process assessment | – | [42] |
|               | 1,4-BDO              | Corn, lignocellulosic residues | GHG, CED | Process assessment | – | [37] |
| Combined TEA and LCA | Methane | Power to gas | GHG | Process design | – | [43] |
|               | Bioethanol           | Rice straw | GHG | Process design | – | [44] |
|               | Biodiesel            | Microalgae | GHG, NER | Process design | – | [45] |
|               | Bioethanol           | Lignocellulosic residues | GHG, CED | Process design | – | [46] |
|               | Biodiesel            | Microalgae | GHG, EcotA, POP, EUAC, LD50 | Process design | – | [47] |
|               | Blendstocks          | Lignocellulosic residues | GHG | Product enhancement | Yes | [48] |
|               | Biodiesel            | Microalgae | GHG | Process optimization | Yes | [49] |
|               | 3-HPA, 1,3-PDO, SA   | Biofeedstock | GHG | Process design | Yes | [50] |
|               | Butanol, ethanol     | Corn stover | GHG | Process design | Yes | [51] |
|               | Biodiesel, glycerol  | Macrogalae | GHG | Process design | – | [52] |
|               | Butanol              | Lignocellulosic residues | GHG | Process design | Yes | [53] |
|               | Phthalic anhydride   | Lignocellulosic residues | GHG, WD, FD | Process design | – | [54] |
|               | Phenol formaldehyde resins | Lignocellulosic residues | GHG, NER | Process design | Yes | [55] |
|               | Higher alcohols      | Ethanol    | GHG | Process design | – | [56] |
|               | 1,3-Butadiene        | Bioethanol and naphtha | GHG, CED | Process design | – | [57] |
|               | Energy and biofuels  | Lignocellulosic residues | GHG, AC, EU, OD | Product selection | – | [58] |
and use of 1 kg of lactic acid, with 99.9% purity, for polylactic acid (PLA) household packaging application in the USA as a functional unit. LCA system boundaries were defined from cradle to grave and TEA system boundaries were defined from cradle to gate (polymerization included).

Table 2. (continued)

| TEA and/or LCA | Chemical or fuel type | Feedstock | Assessed environmental impact category\(a\) | Application/intention of study and stage of development | Early stage | Refs |
|---------------|-----------------------|-----------|---------------------------------------------|------------------------------------------------------|------------|------|
| Biodiesel     | Microalgae            | GHG       | Process design                              | Yes                                                   | [59]       |
| Biogas        | Manure                | GHG       | Process design                              | –                                                     | (A. Shah, dissertation, Iowa State University, 2013) |
| Cellulosic isobutanol, cellulosic ethanol, \(n\)-butanol | Lignocellulosic residues | GHG, EROI, CED | Product comparison | – | [60] |
| Succinic acid and biofuels | Lignocellulosic residues | GHG, LU | Process design | – | [61] |
| Biogas and biofuels | Lignocellulosic residues | GHG, CED | Process design | Yes | [62] |

\(a\)GHG, greenhouse gas emissions; CC, climate change; CED, cumulative energy demand; AC, acidification; EU, eutrophication; OD, ozone depletion; LU, land use; ET, ecotoxicity; HT, human toxicity; MD, mineral depletion; PM, particulate matter; NER, net energy ratio; POP, photochemical oxidation potential; GWP, global warming potential; EcotA, aquatic ecotoxicity; EUAC, carcinogenic emissions to urban air; LD50, median lethal dose; WD, water depletion; FD, fossil depletion; EROI, energy return on investment.

Figure 1. Early-Stage Assessment Framework for Combined Techno-economic Assessment (TEA) and Environmental Life Cycle Assessment (LCA) as a Decision Support Tool in Biotechnology. The framework starts with the acquisition of the relevant raw data, followed by various alignment steps of both assessment methods, then impact aggregation and monetarization, finally aggregated into a single score for decision support.
[7]. Waste handling at the end of life of biochemicals was excluded from the TEA in our simplified example as it is highly dependent on country- or region-specific waste handling technologies, whereas waste treatment impacts during acid production are included in our cradle-to-gate assessment [7].
Figure 3 summarizes our combined TEA and LCA case study results for four scenarios. The scenarios cover three different biofeedstock generations, corn, corn stover, and macroalgae, and for macroalgae we analyzed separately scenarios with and without biomass drying. The environmental sustainability costs (based on LCA results) of corn stover are 46.8% higher than for corn, driven by higher energy demand in feedstock processing. This is mainly due to increased energy consumption for the separation of fiber-rich corn stover biomass (assumed to be done via steam explosion), which is not needed to pretreat corn biomass. We modeled this higher energy demand to be derived 88% from fossil resources matching the current US energy mix [7], which mostly affects damage to human health and natural resources.

Comparing the TEA results for lactic acid produced from corn (first generation) and corn stover (second generation) shows that the economic costs of the second-generation feedstock are 25% lower. Despite lower overall yield, feedstock costs for corn stover are significantly less than for corn. This is influenced by the monetary value assigned to a corn stover unit [63], which will increase significantly with plant size due to transportation and the low fraction of fermentable sugars present in corn stover [12]. Furthermore, the lower level of optimization and TRL of the corn stover process, along with its more fiber-rich biomass composition, requires a more intense separation process, which demands higher chemical concentrations and energy use. Therefore, the energy usage of the second-generation process is one order of magnitude higher than that of the first-generation process. However, this adds only US$0.50/kg produced lactic acid in the TEA results, as utility costs are only a minor contributor to overall TEA results. We emphasize that this example trade-off between lower economic costs but higher environmental costs of corn stover compared with corn can be identified only in a combined TEA–LCA assessment.

Figure 3. Contribution of Monetarized Environmental Impacts and Economic Impact Costs to the Total Cost per Functional Unit of 1 kg of Polylactic Acid (PLA) from Three Different Biofeedstock Generations and Different Process Systems for Macroalgae [7].
When analyzing the results in further detail, we observe that for corn and corn stover, environmental impacts are highest for human health. For corn, these are driven by indirect land-use change, increasing the effect on global warming due to the increased demand for arable land [71]. By contrast, for corn stover these impacts are driven by global warming related to the high energy demand of the biorefinery stage, due to intensive energy use during biomass pretreatment.

Feedstock costs for lactic acid produced from macroalgae (third generation) account for almost 50% of the total economic costs (based on TEA results) (Figure 3). Energy utilities comprise about 20% of these costs, with drying as the main contributing process. Excluding drying results in a decrease in steam use of more than 100 MJ/kg lactic acid, but this has only a low effect on total costs per functional unit due to the low price of steam. However, analysis of the reduction in steam use in the LCA results shows that the related environmental impacts per functional unit are reduced by more than 40%. By comparing the total cost results for macroalgae-based lactic acid production, we can pinpoint the trade-offs between drying and not drying biomass, which a separate application of TEA and LCA would not have revealed.

**Concluding Remarks**

We have described how a consistent combination of TEA and LCA into a single score can support decisions in early R&D stages of biochemical production processes. In addition to combining LCA and TEA, there are other approaches focusing on multi-objective process optimization – for example, Pareto-based process optimization, usually called non-dominated or non-inferior [72] – or data envelopment analysis focused on evaluating relative efficiency [73]. However, while such approaches might provide more objective results than a single score, they are often hard to interpret for decision makers.

With growing needs for chemicals that are aligned with global sustainable development goals and circular economy targets [74], industrial biotechnology can benefit from early-stage assessments that guide the development of biochemicals that are both economically and environmentally sustainable. In this context, Figure 3 demonstrates that it is important to develop microbial fermentation strains that can feed on non-dried macroalgae without lowering biomass yield. Results from this assessment framework, with different scenarios, can furthermore help to identify to what extent conversion yields to lactic acid or fermentation productivity are relevant when considering both economic and environmental sustainability. These combined results from the proposed assessment framework could serve as a yardstick by research organizations and companies to rank biochemical development projects based on their combined TEA and LCA performance. Furthermore, our framework could be applied iteratively to optimize entire production schemes with respect to a viable biochemical production idea from both an economic and an environmental sustainability perspective.

Identifying combined economic and environmental hotspots provides insights into costs that could be mitigated by the adoption of certain strategies early in the biochemical development process. Energy-associated costs appear as a hotspot in TEA and LCA across our case study scenarios. For example, for macroalgal feedstock, drying the biomass has the biggest effect on energy use (accounting for more than 50% of the energy utilities). Removing macroalgal drying affects the TEA results by only 7%, but indirect LCA-related costs from energy use are reduced by 61% in countries relying on fossil fuels as main source for energy [7].

Overall, we have highlighted that it is crucial to account for both economic and environmental sustainability aspects to optimize the overall performance of biochemical production, which provides the foundation for increased market competitiveness. This can be accomplished by...
considering aligned systems (i.e., the same process unit operations and energy and materials balances), using a comprehensive set of indicators to cover all product life cycle stages, and expressing TEA and LCA results in comparable units. While many research questions remain to be addressed to develop biochemicals (see Outstanding Questions), we hope that our proposed assessment framework can help the bioeconomy to become economically viable and environmentally sustainable in line with global sustainability targets and market goals.

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