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# Regular article Aeration costs in stirred-tank and bubble column bioreactors

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# **1. Introduction**

Since the development of penicillin production by submerged aerobic cultivation of *Penicillium chrysogenum*, aerobic biological production ("aerobic fermentation") has been used to produce an increasing variety of chemical products [1]. The range of products being produced or considered for biological production has grown rapidly with recent advances in metabolic engineering, synthetic biology and bio-based production technologies [2,3]. Owing largely to the relatively high cost of supplying molecular oxygen  $(O_2)$  to a submerged culture, aerobic fermentation has historically primarily been applied to produce lower volume, higher value (higher margin) compounds like pharmaceuticals and specialty chemicals. The challenges to achieving economical aerobic production become greater for larger volume, lower margin products where material and utility costs generally dominate fermentation economics [4]. The higher capital and operating costs for aerobic production are well recognized [5,6] and are also stimulating research and development on anaerobic routes for biological production. [7,8]. Cost constraints become the most acute for economic aerobic production of extremely low-margin, high-volume commodity products like biofuels, and this motivated us to assess aeration costs for large-scale aerobic production in the context of such products.

Aerobic fermentation is a critical unit operation in the process of making fuel-range hydrocarbons from sugars, when the hydrocarbon or its precursor, e.g., a lipid or free fatty acid, is directly produced in

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# ABSTRACT

To overcome knowledge gaps in the economics of large-scale aeration for production of commodity products, Aspen Plus is used to simulate steady-state oxygen delivery in both stirred-tank and bubble column bioreactors, using published engineering correlations for oxygen mass transfer as a function of aeration rate and power input, coupled with new equipment cost estimates developed in Aspen Capital Cost Estimator and validated against vendor quotations. These simulations describe the cost efficiency of oxygen delivery as a function of oxygen uptake rate and vessel size, and show that capital and operating costs for oxygen delivery drop considerably moving from standard-size  $(200 \text{ m}^3)$  to world-class size  $(500 \text{ m}^3)$  reactors, but only marginally in further scaling up to hypothetically large  $(1000 \text{ m}^3)$  reactors. This analysis suggests bubble-column reactor systems can reduce overall costs for oxygen delivery by 10–20% relative to stirred tanks at low to moderate oxygen transfer rates up to 150 mmol/L-h.

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submerged culture by a microorganism. However, little public domain information exists about state-of-the-art designs and economics of large-scale aerobic bioprocesses, especially for those producing low-margin, commodity products like biofuels where extreme cost minimization is required. Previous techno-economic analysis (TEA) reports from the National Renewable Energy Laboratory (NREL) [9–11] demonstrated that, in the case of cellulosic ethanol, the fermentation area (comprising mechanically simple but extremely large anaerobic fermentation vessels up to  $10^6$  gallons) was not a primary cost contributor, generally falling behind larger cost drivers including biomass pretreatment, cellulase enzyme production/purchase, and wastewater treatment. A more recent TEA report [12] examined the aerobic conversion of lignocellulosic sugars to hydrocarbons by way of a fatty acid intermediate. In contrast to the earlier ethanol analyses [12], concluded that the aerobic fermentation area *was* a primary cost contributor for integrated cellulosic biofuel production; in fact, it was the largest contributor of all process areas, with fermentation compressors and agitators also representing the largest power demand in the biorefinery process.

As the first publicly available TEA for such a technology pathway, the [12] analysis carried a higher degree of uncertainty in its underlying process design and capital cost assumptions than more established pathway concepts. Key among such uncertainties were the operating conditions, performance parameters, and cost contributions of the aerobic fermentation step. Parts of the process design were supported by a partner engineering company, which provided initial input on the design of stirred-tank aerobic bioreactors, and associated capital cost estimates. Since publication, this design has been reviewed by several engineering companies and consultants, including Harris Group, Katzen International, Benz Technologies, and Geno

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matica. Following these critical reviews, it was concluded that several assumptions pertaining to the operational performance and capital costs used in [12] erred on the optimistic side for commercial-scale aerobic fermentation.

This article documents efforts to reduce uncertainty in such key process and cost parameters through (1) development of an independent framework for bioreactor cost estimation that is validated against high-quality vendor quotes and (2) modeling of low-viscosity, aerobic fermentation using simple design equations and a steady-state process simulator, to understand achievable oxygen transfer rates as a function of vessel configuration, power input, and aeration rates. Together, these developments will be used to guide future refinements in conceptual design and TEA of biochemical conversion processes.

# **2. Calculations**

# *2.1. Bioreactor capital cost estimation*

Ideally, well validated TEA studies should favor direct capital equipment inputs/quotations from equipment vendors, especially for critical and costly items like fermentors. However, external estimates are not always readily obtained for conceptual studies and can be scattered and sometimes conflicting. To facilitate rapid comparative analysis across multiple technology options, methods for consistent estimation of bioreactor capital costs were developed using Aspen Capital Cost Estimator (ACCE). ACCE estimates costs for individual equipment items using volumetric models (as opposed to factored models), which compute total estimated materials and labor involved in building a piece of equipment based on its specified size. For example, if a specified vessel is too large or heavy to be transported in one piece (and all the vessels considered in this article are), ACCE will compute costs for shop fabrication of transportable pieces and costs for final field fabrication, all as part of a total bare equipment cost. A variety of high-quality bioreactor quotes obtained over recent years from vendors and engineering firms were used to create general guidelines for specifying fermentation vessels in ACCE, resulting in reasonably accurate, absolute capital cost predictions for both stirred-tank reactors (STRs) and bubble-column reactors (BCRs).

With these specification guidelines, a set of capital costs for STRs and BCRs were developed at different standard vessel volumes. Economies of scale naturally dictate use of the largest reaction vessel possible; however, while million-gallon (3800 m<sup>3</sup>) *anaerobic* fermentors are in use at industrial fuel ethanol plants, the maximum practical *aerobic* reactor volume is less clear. Our industry contacts have intimated that the largest STRs in operation are in the hundreds of cubic meters  $(\leq 500 \text{ m}^3)$  and their ultimate maximum size must be on the order of  $1000 \text{ m}^3$ , owing to diminishing returns on oxygen transfer relative to volumetric power input, as well as practical limitations regarding the fabrication and maintenance of very large impellers, shafts, bearings, and motors. Bubble columns are not limited by moving parts and BCRs up to 1000  $m<sup>3</sup>$  are known to be in operation [6]. Costs were therefore estimated for BCRs and STRs at three standard vessel sizes, with the understanding that uncertainty in cost increases with vessel size:

- $\cdot$  200 m<sup>3</sup>, representing an "off-the-shelf," readily purchasable reactor.
- 500 m<sup>3</sup>, representing a "world's-largest" class of reactor that exists in relatively small numbers.
- $\cdot$  1000 m<sup>3</sup>, representing a "hypothetically large" reactor that may or may not exist today, representing a ceiling for what is likely viable from a design and operational standpoint.

# *2.2. Flowsheet simulation of aerobic fermentation*

To accompany the new standard bioreactor capital costs, we carried out steady-state flowsheet simulations in Aspen Plus to investigate the operating costs associated with aeration power demand. Fig. 1 depicts the general bioreactor schematic considered here, equally applicable to STR or BCR vessels aside from the depicted agitator; a bioreactor is part of a complex of interacting energized systems, including an agitator (for STRs, eliminated for BCRs), an air compressor with discharge cooler, and a chilled-water system for temperature control, itself connected to a larger cooling water system. The system shown in Fig. 1 uses forced-circulation heat removal, but jackets or coils may be favored instead, depending on sterility and shear stress concerns. Aspen Plus simulations of STRs and similarly-equipped BCRs of 200, 500, and  $1000 \text{ m}^3$  were performed to



**Fig. 1.** Flow diagram of a single STR and support equipment. The flow diagram for a BCR is identical, except for elimination of the agitator.

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determine the total system power demand for most of the users shown in Fig. 1: air compressor, air cooler, agitator for STRs, circulation pump, and chiller (scaled by cooling duty). The cooling tower was not included because its power contribution is insignificant compared to the chiller.

The independent variable determining total system power was taken to be the oxygen uptake rate (OUR). In an operating bioreactor, the submerged culture provides some OUR, which, at steady-state, is equal to an oxygen transfer rate (OTR); the product of a mass transfer coefficient, *k<sup>L</sup>* , a mean bubble specific interfacial surface area, *a*, and an oxygen concentration driving force,  $(C^* - C_L)$ :

$$
OUR = OTR = kL a (C^* - CL)
$$
\n(1)

where  $k_L a$  is usually lumped together and  $C^*$  and  $C_L$  are respectively the equilibrium and the actual dissolved oxygen concentrations (mmol/L). For reactor design purposes, several literature correlations are available to relate  $k<sub>L</sub>a$  to fundamental operating parameters. In STRs, the non-viscous mass transfer correlation of [13] is frequently used as a design equation. This correlation describes  $k<sub>L</sub>a$  as a function of bioreactor gassed power input  $(P)$  per unit volume  $(V)$  and the gas superficial velocity within the reactor,  $u<sub>S</sub>$ :

$$
k_L a \, [\text{s}^{-1}] = 0.002 \, (P/V \, [\text{W/m}^3])^{0.7} \, (u_S \, [\text{m/s}])^{0.2} \tag{2}
$$

where the pre-factor and exponents are adjustable for specific systems. This correlation is often relied on for its simplicity, as it does not depend on specific reactor geometry, or impeller speed, number, and type (though the accessible range of *P/V* is an implicit function of these [14]). The review of [15] lists other, more complex, correlations for  $k<sub>L</sub>a$ , but notes that the original Van't Riet correlation (Eq. (2)) is the most frequently used for basic design in non-viscous systems. Reactor sizes  $>100 \text{ m}^3$  are out of the fit space for the original correlation, but [16] developed a zoned model where the correlation was applied independently to stirred and unstirred zones within a larger reactor, and concluded that in the limit of good mixing  $(1/k<sub>L</sub>a > t<sub>mix</sub>)$ , the correlation could be simply applied to the entire volume. In any event, well proven correlations like Eq. (2) can be used to determine idealized scaled-up aerated bioreactor scenarios and make cost predictions.

For BCRs, [17] proposed a similar correlation, with  $k<sub>L</sub>a$  a primary function of the gas superficial velocity only. [13] further described how this correlation can be corrected for temperature, *T*, and effective broth viscosity, *meff*, resulting in:

$$
k_L a \, [\,\mathbf{s}^{-1}\,] = 0.32 \, (u_S \, [\,\mathbf{m/s}\,])^{0.7} \, (m_{\text{eff}} \, [\,\mathbf{c} \mathbf{P}\,])^{-0.84} \times 1.025^{(T^{\circ} \mathbf{C}) - 20)} \tag{3}
$$

It should be noted that BCRs are not normally recommended for fermentations where the broth viscosity is higher than 2 cp. We therefore limit our comparisons to non-viscous (aqueous) systems in the scope of this study.

In aerobic cultures where molecular oxygen  $(O_2)$  is the primary electron acceptor at the end of the electron transport chain, it can be shown that the heat of reaction is proportional to the oxygen uptake rate, regardless of the actual effective stoichiometry or products of the culture [18]. Approximately 110 kcal of heat is released per g-mol  $O_2$  consumed, which is equivalent to the heat of reaction (on an  $O_2$ )

basis) of the glucose combustion reaction  $(C_6H_1, O_6 + 6 O_2 \rightarrow 6$  $CO<sub>2</sub> + 6 H<sub>2</sub>O$ . Thus, rather than assume a specific biological system/ product in the Aspen Plus simulation, OUR is simply taken in this work to be a volumetric rate of combustion of glucose by oxygen, in the liquid phase, in units of mmol  $O_2$  consumed per liter per hour (mmol/L-h). For a given OUR, the simulation computed OTR from the aeration rate using Eq. (1) and the correlation in Eq. (2) (STRs) or Eq. (3) (BCRs). The inlet air rate was then varied to set OTR equal to OUR. The STR correlation lends itself to power optimization between agitator power and gas superficial velocity (and compression); an optimization routine was used to vary these simultaneously to find the minimum total power for a given OUR. The BCR correlation cannot be similarly optimized, i.e., there is only a single  $u<sub>s</sub>$  (and thus a single power) for a given OUR.

Simulations were run at steady state with stoichiometric glucose feed rate determined by OUR and vessel size. The reactor was modeled as a RSTOIC reactor block with flash vessel for vapor/liquid disengagement.  $CO<sub>2</sub>$  and water formed in the combustion reaction were removed via the vent and liquid product streams. Air was supplied through a compressor with discharge pressure determined by the liquid head in the reactor, plus line losses. The inlet air was 70% saturated with water to avoid a significant makeup flow due to evaporative stripping by the sparged air. The reactor block ran adiabatically with outlet temperature maintained at 32 °C by continuous pump-around circulation of the liquid through a heat exchanger with a 20 °C outlet; as noted above, depending on the specific needs for a given production organism, e.g. regarding sterility or shear stress concerns, alternative designs for temperature control may be appropriate such as vessel jacketing. This cooling loop removes all heat produced by the combustion reaction as well as (for STRs) the heat generated in dissipating agitator power (applied power less drive and bearing inefficiencies) [19]. The chiller duty was converted to power using a rule of thumb of 1.24 hp/ton refrigeration [20].

Due to the high circulation rate, both BCRs and STRs were assumed to be well-mixed and an overall concentration driving force was taken to be the log-mean average between the well-mixed  $O_2$ concentration and the Henry-saturated concentrations at the bottom and top of the reactor. This is an important limitation of the model; the steady-state, well-mixed, dissolved  $O_2$  concentration is implicitly a function of OUR and thus cannot be set independently. In practical batch or fed-batch bioreactor operation, aeration and agitation would be controlled along with substrate and nutrient feed rates to keep the dissolved  $O_2$  concentration near zero, where mass transfer is most efficient. Moreover, in practice for a biological system, OUR may be highly variable over the course of a fermentation cycle between cell-growth versus product (e.g. lipid) accumulation stages, further confounded by changing liquid levels in fed-batch operation; such variables are not part of the intended focus of this paper which models a fixed-volume batch operation with all solubilized oxygen converted via a generic combustion reaction. Additionally, in a biological system with high OURs and also high vessel fill levels, flooding of liquid out the vent could become a concern, which would need to be addressed through appropriate maximum fill thresholds (minimum vessel headspace) and/or antifoam agents (again, beyond the scope of this analysis, where all cases assumed a fixed 80% ungassed working volume). A dynamic model (in preparation) will permit more sophisticated study of these issues and associated economics; the steady-state model, however, affords strong conclusions about conceptual process configuration and bioreactor selection.

#### **3. Results and discussion**

#### *3.1. Bioreactor capital costs*

Table 1 details four comparisons between vendor quotes obtained by NREL and costs estimated with ACCE, for medium- to large-scale STRs and BCRs and one extremely large anaerobic ethanol fermentor. Only costs for bare vessels (no agitators) are compared. The "vertical process vessel" item from the ACCE equipment library was used for BCRs and bare STRs. The million-gallon anaerobic fermentor was approximated with the "flat bottom storage tank" item, which it more closely resembles physically. Metallurgy and design pressures are key to cost estimation because ACCE computes vessel

#### **Table 1**

Comparison of bioreactor cost quotes obtained from vendor/EPCs and costs estimated with ACCE (2014\$).

Description	<b>Ouoted Specs</b>	Ouote	<b>ACCE</b> Specs	ACCE cost
1 MMgal anaerobic fermentor (bare vessel)	304SS shell $55¢$ diam. $X 53¢$ height Atmospheric pressure	\$907,000	Storage tank, cone roof 304SS shell 55¢ diam. X 53¢ height 5 psig	\$911,000
$200 \text{ m}^3 \text{ STR}$ (bare vessel)	304SS shell $15¢$ diam. $X 40¢$ height $-0.5$ to 1 psig	\$356,000	Vertical process vessel 304SS shell $15¢$ diam. X $40¢$ height Vacuum to 45 psig	\$383,000
$300 \text{ m}^3$ STR (bare vessel)	316SS shell $300 \text{ m}^3$ , $2.7:1 \text{ H}$ D Atmospheric pressure Internal cooling coil	\$442,000	Vertical process vessel 316SS shell 17¢ diam. X 45.5¢ height $0-45$ $psi + 20%$ allowance for internals	\$440,000
$670 \text{ m}^3$ BCR	316SS shell $670 \text{ m}^3$ , 6:1 H/D Vacuum to 45 psig Jacketed	\$1,900,000	Vertical process vessel 316SS shell 17¢ diam. X $100¢$ height Vacuum to 45 psig Half-pipe jacket in A204C	\$2,040,000

#### **Table 2**

Vessel specifications and capital costs for STRs and BCRs estimated with ACCE (2014\$).



thickness (and therefore vessel weight) from these. In storage tanks, which ACCE assumes to be liquid-full, only the pad pressure is required. In process vessels, which are not full by default, an allowance should be added for head pressure at the vessel bottom. In steam-sterilizable vessels, design for vacuum is required by code; this requires stiffening rings inside the vessel. In ACCE, these rings add essentially the same cost at low vacuum and full vacuum. As seen in Table 1, from a limited number of details about a vessel, and some general specification guidelines, it is thus possible to achieve reasonable cost agreement with vendor quotes by correctly specifying an analogous vessel in ACCE.

Using these guidelines, and a preference for 316 stainless steel, Table 2 presents costs for bare vessels in the standard sizes discussed in Section 2.1, along with relevant specifications provided to ACCE. Vessel perforations (e.g., nozzles and manholes) and their associated connection flanges can have a large effect on the vessel weight and therefore its cost, so these are presented as well. The STR costs in Table 2 do not include agitators. As the agitator power increases, however, the total reactor cost must increase as well, due to larger motors, gear boxes, and associated stabilizing infrastructure. ACCE captures this cost increase, as shown in Fig. 2, which presents the total costs of vessel and agitator for the three STR sizes in 316SS at motor powers from 10 to 2,500 hp. The ACCE "agitated tank-enclosed" equipment item was used to generate these costs.

# *3.2. Total cost of aeration*

Fig. 3a shows the power required to deliver a kilogram of oxygen in STR and BCR systems for the three vessel sizes and OURs ranging from 10 to 150 mmol  $O_2/L$ -h. (BCRs are generally not considered above 150 mmol/L-h, due to jet flooding at high gas velocity.) For STRs, Fig. 3a indicates that the specific  $O<sub>2</sub>$  delivery power is nearly constant; this is in part due to the optimization of agitation and aeration powers. Furthermore, the power required to achieve a given OTR does not change significantly with vessel size (the difference between 500  $\text{m}^3$  and 1000  $\text{m}^3$  is less than 5%). For BCRs, there is a more pronounced increase for gassing power input over the same OTR range, as OTR is only controlled by aeration rate and higher

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**Fig. 2.** Capital costs (uninstalled, 2014\$) of STRs in 316SS as a function of agitator power.

compression power is required for larger volumes of air. The power scales slightly more favorably with volume at higher OTR, with a 10% power reduction between 500  $\text{m}^3$  and 1000  $\text{m}^3$ . In either case, for large reactors at a given OTR, the total bioreactor system power varies approximately linearly with total liquid volume. This implies that any beneficial economies of scale realized at larger vessel sizes are more strongly a result of reduced capital costs for the vessels and agitators than reduced operating costs resulting from differences in power demand or cost efficiency.

To investigate the economies of scale possible for aeration, capital and operating costs were incorporated into the analysis. The bioreactor capital costs were taken from ACCE as discussed above. For STRs, these were obtained from Fig. 2 as a function of optimized agitator power. A fixed installation factor of 2.3 was used to obtain a total direct cost for the bioreactors. Capital costs for compressors, pumps, and heat exchangers were also estimated with ACCE, though these were generally small compared to the reactor cost. The total capital cost was then converted to an amortized fixed cost  $(\frac{6}{h})$  using a 13% annual capital charge factor and 8400 operating hours per year, consistent with NREL's cash flow calculation methodologies, e.g., as published in [12] and [10]. Operating costs were calculated as the sum of electricity at \$0.06/kWh and maintenance at 6% of total installed capital. The resulting aggregate OPEX plus amortized CAPEX costs were combined with the oxygen delivery rate required for each combination of OUR and vessel size, yielding a  $\frac{f}{g}$  /kg  $O_2$  cost, shown in Fig. 3b. This can be thought of as the total cost to deliver a kg of oxygen to a culture, for a single reactor and the associated equipment depicted in Fig. 1. Fig. 3c shows the same data plotted in terms of the total annual cost required to operate the system in Fig. 1 (total cost of ownership), normalized by reactor volume  $(\frac{f}{y-m^3})$ . Note that the cost of substrate (glucose) has not been included in Fig. 3b–c; substrate cost of course increases linearly with OUR, and has been omitted here to focus on the cost efficiency of  $O<sub>2</sub>$  delivery, which is primarily a function of power.

There are several conclusions to be drawn from the curves in Fig. 3b–c. First, with the  $k<sub>L</sub>a$  correlations used and over the OUR range studied, BCRs are always less expensive to operate than STRs of the same size, with larger savings at lower OUR. Van't Riet (1991) reached an analogous conclusion in a similar analysis (see Example 18.3). Depending upon the cost metric assessed,  $\frac{1}{2}$  /kg O<sub>2</sub> supplied (Fig. 3b) or  $\sqrt[6]{y-m^3}$  (Fig. 3c), use of BCRs reduces overall aeration costs by 10–20% relative to STRs, assuming the process is suitable for implementing in a BCR. Second, for both reactor types there is a significant cost advantage in scaling up from 200 to 500  $\text{m}^3$  and a rel



**Fig. 3.** (a) Specific total power demand, (b) specific aggregate capital and operating cost and (c) annual aggregate capital and operating cost to deliver oxygen in STR and BCR systems at varying vessel volume and OUR.

atively smaller advantage in further scaling up from 500 to  $1000 \text{ m}^3$ . This effect may be larger in the context of a whole-plant analysis, since the aggregate costs in Fig. 3b–c do not include manpower, which should naturally decrease with a smaller number of larger reactors. Third, specific oxygen delivery cost flattens out near an OTR of roughly 50–75 mmol/L-h, for all reactors, indicating that the cost efficiency of delivering  $O_2$  is better at higher OTR up to this limit. Finally, Fig. 3b indicates there is likely little incentive to make a bioreactor larger than  $1000 \text{ m}^3$ . Beyond the physical limitations discussed earlier, the diminishing economies of scale are unlikely to justify development of such a large unit.

The above observation that  $O<sub>2</sub>$  delivery is more cost-efficient at moderate to high OTR has implications for the production of high-volume commodities like bulk chemicals and biofuels where extreme cost minimization is essential for techno-economic viability. For example, to make the most efficient use of fermentor capital equipment, it is important to be able to obtain and maintain a high volumetric productivity during the production phase of the target product. For chemical or fuel precursors produced aerobically at high productivity, the OTR requirements can be significant. The techno-economic trends shown here are encouraging, as they indicate that higher-OTR processes are more cost-efficient. Nonetheless, substantial challenges remain to making biofuels cost effectively via aerobic routes [21].

The trends established from the analysis and methodology presented here will help to define optimal operating conditions for future detailed models of aerobic processes, e.g., favoring BCRs over STRs where possible, and assuming bioreactor sizes of  $500-1000$  m<sup>3</sup>. For low-margin, commodity fuels and chemicals processes, BCRs are likely more cost-effective than STR vessels based both on the present analysis as well as feedback from industry. For processes not amenable to BCRs, an optimum STR design would likely be based on a 500 m<sup>3</sup> vessel volume operating at an OTR above 50 mmol/L-h. Although slight cost improvements may be seen going to larger volumes, such reactors would be larger than commercially available units today.

#### **4. Conclusions**

Uncertainty in aerobic bioreactor capital and operating costs in conceptual process design and TEA remains largely inevitable as many biological parameters, including oxygen transfer requirements, are generally not firmly established at the time of analysis. The methods described here help to reduce uncertainty by validating software capital cost estimates against high-quality vendor quotes and by using simple design equations in a steady-state process simulator to assess the cost efficiency of oxygen delivery in different vessel configurations. Vessel metallurgy and design pressure are the keys to accurate cost estimation, and significant cost efficiencies can be realized by favoring BCRs over STRs, at a maximum bioreactor size of  $500-1000$  m<sup>3</sup> and OTR between 50 and 150 mmol/L-h.

These observations will inform future detailed models of aerobic production. As researchers at NREL and elsewhere continue to identify aerobic cultures and optimize their performance, a theory-based economics approach such as the one presented here can be used to guide research.

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