Evaluating and Guiding the Development of Sustainable Biorenewable Chemicals with Feasible Space Analysis

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ABSTRACT

The economic and environmental performance of a biorenewable chemical process is analyzed by defining its cost, energy, and greenhouse gas feasible design spaces in terms of process parameters. Delimiting the feasible space of a process allows developers to set development targets and quantify performance trade-offs among unit processes. Feasible space analysis is demonstrated for the biocatalytic synthesis of C10 saturated fatty acid from glucose. Capric acid yield from glucose of $\geq 0.25 \text{ g g}^{-1}$, titer of $\geq 40 \text{ g l}^{-1}$, and volumetric productivity of $2 \text{ g l}^{-1} \text{ h}^{-1}$ are found to result in cost, greenhouse gas emissions, and energy consumption as good as or better than the conventional process for production of fatty acids from coconut oil.

Key words: Biocatalysis, Biomass conversion, Process development, Feasible space, Fatty acid, Sustainability

1. Introduction

There is growing interest in biorenewable chemicals because of their perceived economic and environmental benefits [1]. It is expected that production from renewable, plant-derived sugars should, in the long-run, allow a low cost of production relative to conventional petrochemicals. Environmental benefits are also expected through the use of biorenewable feedstocks, particularly in terms of carbon footprint. Unfortunately, none of these benefits are certain and recent biorenewable chemical investments have included some high-profile disappointments [2]. To avoid such disappointments, the economic potential and environmental sustainability of a new biorenewable chemical production process should be determined before large irreversible investments are made in process development and scale-up to production scale.

The techno-economic analysis (TEA) and life cycle assessment (LCA) methods are often used to assess the economic and environmental performances of new chemical processes [3,4]. One process configuration or a single combination of process parameters (yield, selectivity, etc.) is usually evaluated when assessing the potential of a new chemical process [4]. If such analyses indicate that a process is not economically viable and environmentally sustainable, then further development may be stopped. The economic and environmental feasibility of a new chemical process, however, still may be achieved by further improvement of the process. It is, therefore, necessary to assess the performance of a new chemical process over a range of combinations of process parameters in order to determine the combinations that would be economically and environmentally feasible. In this manner, one can avoid eliminating processes that are currently unviable but could potentially be made viable. Knowledge of which combinations of process parameters would make the process viable can guide the efforts of process development teams,

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4 allowing them to focus on improving those process parameters that, on the basis of the current
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6 stage of technology, are not in the feasible range.
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9 A new biomass conversion technology (biological, chemical, and thermo-chemical) has
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11 to pass through multiple stages of process development (laboratory-, pilot-, and demonstration-
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13 scale) before it is implemented at commercial scale. Often the transition from early research to
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15 commercialization takes 10 years or more and requires large capital investment [5]. Reducing
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17 technology development time will enable faster access to markets. Technology development can
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19 be accelerated by coordinating efforts between multiple development teams working on different
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21 process technologies, such as catalytic conversion and separations. In this case, the economic
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23 performance of a new chemical process might be improved by developing a separation process
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25 that can be used to easily recover and recycle unconverted raw material, if it is difficult to
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27 improve the catalyst conversion. Technology development efforts tend to have an asymptotic
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29 return on investment, such that the economic benefit per dollar invested in improving process
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31 performance grows smaller. Determining the economic benefits of improving process parameter
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33 values will allow research and development teams to focus on improving those process
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35 parameters that have the potential to provide better economic performance.
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43 A semi-quantitative method has been proposed by Patel et al. [6] that integrates economic
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45 and environmental indicators to provide a generic ‘feasibility score’ that is useful as a way to sift
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47 through many novel biorenewable chemical routes early in the development process [6]. This
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49 method, however, is not used to quantitatively assess the economic viability of a process for the
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51 production of the biorenewable chemical over a range of process parameters and to determine
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53 process trade-offs among process parameters. Understanding the consequences of process trade-
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55 offs allows the setting of meaningful performance targets for the technology development team.
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4 This paper provides a new approach by combining feasible space analysis (FSA), TEA, and LCA
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6 methods to evaluate and guide the development of biorenewable chemical technologies. The
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8 shortcomings of existing approaches for the assessment of biorenewable chemical production
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10 processes can be overcome by combining these methods.
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14 The FSA method maps the trade-offs in process parameters into production performance
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16 metrics, such as the production cost of a process. Such a mapping defines a “space” of process
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18 parameters that will result in a commercially viable process for chemical production. The FSA
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20 method has been used to optimize the cost performance of chemical processes [7,8]. In addition
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22 to cost considerations, new and existing chemical production processes must meet environmental
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24 objectives, as there is a growing concern over the increasing greenhouse gas (GHG)
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26 concentrations in the atmosphere [9]. Therefore, it would be useful to extend the FSA method to
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28 take environmental objectives into account, which has not been done before.
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33 We used the minimum selling price (MSP) as an economic performance metric, and
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35 energy consumption and GHG emissions as environmental performance metrics [10]. The MSP
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37 of a biorenewable chemical that is synthesized using a biocatalyst, for example, is driven by the
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39 costs of feedstock, fermentor, and separations [11]. Feedstock cost is dominated by the yield of
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41 chemical per unit of feedstock and the price of feedstock [12]. The separations cost is driven by
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43 the product titer [13]. The production rates influence the capital and operating costs of the
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45 fermentor [14]. Similar to the MSP, the GHG emissions and the energy consumption of a
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47 biocatalytic process are largely influenced by productivities, titers, and yields. The feedstock
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49 production might cause the largest life cycle environmental impact in the biorenewable chemical
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51 production system. The yield determines the amount of feedstock required for making the
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53 chemical and thus the feedstock contribution to the overall energy consumption and GHG
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emissions. The energy requirement of the fermentation process depends on the agitator power (kW), which, in turn, depends on production rates. The fermentation titer impacts the energy demand and GHG emissions of downstream processes.

In the current work, the production of fatty acid from glucose using *Escherichia coli* (*E. coli*) was used as a model system to demonstrate the assessment of a new biorenewable chemical process by combining the methods of FSA, TEA, and LCA. Fatty acids are platform molecules that can be transformed into a range of industrial chemicals, such as fatty alcohols [15], α -olefins [16], ethyl esters [17], and alkanes [18]. Global consumption of fatty acids is increasing at a rate of 3% annually [19]. Currently, fatty acids are primarily made from natural oils, such as coconut oil [20]. The hydrolysis of these natural oils results in a mixture of fatty acids that is further fractionated into pure fatty acids. The environmental impact of conventional fatty acid production is high, as the fractionation process consumes large amounts of fossil energy [20]. The new market opportunities for fatty acids and negative environmental impacts of the conventional process have driven interest towards developing efficient biocatalysts to synthesize fatty acids from sugars [21]. Producing fatty acids in a microorganism would allow tailoring properties, such as chain length and functionality, which can add special value by addressing the needs of specific industries, such as the detergent industry [22].

In this work, capric acid was used as a model fatty acid molecule. A process flow diagram (PFD) for the synthesis of capric acid was developed. The PFD was modeled to determine material and energy balances of the capric acid production process for various combinations of yield, titer, and volumetric productivity. These balances were used to estimate MSP, energy use, and GHG emissions of the capric acid production process. Such estimates were utilized to generate cost, energy, and GHG performance surfaces. Finally, a feasible space

for the glucose-based capric acid production process in terms of yield, titer, and productivity was defined using performance surfaces and constraint planes of cost, energy, and GHG. The constraint planes were determined by estimating performance metrics of the coconut-oil-derived capric acid production process. The assessment of glucose-based capric acid production by combining FSA, TEA, and LCA indicated that this process has the potential to compete with the conventional technology in terms of economic and environmental performances. However, the biocatalyst development team must achieve capric acid yield from glucose of greater than 0.25 g g⁻¹ and a titer greater than 40 g l⁻¹ if the process is to meet the performance of the conventional technology in terms of cost, energy use, and GHG emissions.

2. Process Description and Modeling

In the patent published in 2014 by San and Han, a strain of *E. coli* was used to synthesize capric acid from glucose [21]. The biocatalyst development team has attained a capric acid yield of 0.25 g g⁻¹, a volumetric productivity of 0.8 g l⁻¹ h⁻¹, and a titer of 15 g l⁻¹ (personal communication from the development team). We created a PFD of this process (Fig. 1). An annual plant capacity of 40,000 metric tons of glucose conversion and a plant life of 20 years were assumed. The PFD has three major sections: seed fermentation, product fermentation, and separation/purification, which are described in detail in the following subsections.

2.1 Seed fermentation section

The *E. coli* strain is cultivated under microaerobic conditions on Luria Bertani (LB) medium in a seed fermentation train consisting of a series of fermentors [23]. The first fermentor in the seed fermentation train, with a volume of 10 L, is inoculated with an *E. coli* cell culture grown in a 1-L laboratory-scale fermentor. After the cells reach a particular density, the cell broth is transferred to the next reactor in the seed fermentation train, and so on. After attaining

the required cell density for the inoculation of the production fermentors, the *E. coli* cell broth from the final seed reactor is sent to the production fermentor.

SuperPro Designer® simulation software was used to simulate the seed fermentation train. The material and energy balances and the volumes of seed fermentors were estimated from these simulations. The growth of *E. coli* in the seed fermentation train was modeled using conventional Monod kinetics. A value of 0.4 h^{-1} was used for the maximum specific growth rate. The yield coefficient of biomass from glucose was taken as $0.5 \text{ (g dcw) (g glucose)}^{-1}$. The seed reactors were assumed to be operating in batch mode with a turnaround time of 6 h [24].

2.2 Product fermentation section

The microbial inoculum from the final fermentor of the seed fermentation train is fed to the production fermentor. The production fermentor is operated in fed-batch mode by feeding glucose. In the production fermentor, *E. coli* synthesizes capric acid from glucose and secretes it into the fermentation broth. The production of capric acid is carried out under microaerobic conditions on minimal medium. The temperature of the production fermentor is maintained at 37°C . A base is added to the fermentor to maintain a pH of 5 as the production of capric acid would otherwise cause a decrease in pH.

The production fermentor was modeled using SuperPro Designer® to estimate its volume. Capric acid was assumed to be a fully growth-associated product (i.e., the specific rate of capric acid production is directly proportional to the specific growth rate) [25]. The values for maximum specific growth rate, biomass yield, and capric acid yield were taken as 0.1 h^{-1} , $0.05 \text{ (g dcw) (g glucose)}^{-1}$, and $0.38 \text{ (g) (g glucose)}^{-1}$, respectively.

2.3 Separation and purification section

The fermentation broth containing capric acid, water, nutrients, and other impurities is sent to a rotary vacuum filter (RVF). We modeled a RVF with a microporous filter medium, such as a membrane filter, and with the use of diatomaceous earth as a filter aid to remove *E. coli* cells from the fermentation broth [26-28]. A filtration time of 30 h, a filtration flux rate of $250 \text{ l m}^{-2} \text{ h}^{-1}$, and a filter cake level of dryness (LOD) of 30 were used in the modeling of the RVF, using SuperPro Designer®. The retentate of filtration, containing microbial cells and other solids, is discharged as a waste stream. The flow rates of retentate and filtrate and filter membrane area were estimated using cake dryness and filtration time data.

The capric acid can be extracted from the clarified fermentation broth by solvation with *n*-hexane. The reader is referred to the supplementary information about details of the solvent selection criteria and the modeling of the solvent extraction process. SuperPro Designer® was used for the simulation of the solvent extraction column. The volumetric flow rates of the raffinate and extract phases of the column, the diameter of the column, and the number of stages were estimated from the simulation.

The extract phase, containing *n*-hexane, capric acid, and a very small amount of water, is sent to a distillation column. Distillation is utilized to recover the *n*-hexane. The *n*-hexane and water mixture is collected as a condensate at the top of the distillation column. This mixture is recycled to the solvent extraction column. The capric acid is recovered from the reboiler at the bottom of the distillation column. Aspen Plus® was used to simulate the distillation column because it provides sophisticated models (such as RadFrac) that can be used to model distillation columns rigorously.

The very small amount of *n*-hexane, dissolved in the continuous phase of the solvent extraction column, can be recovered using an evaporation column or a decanter. The top vapor stream of the evaporation column containing *n*-hexane is sent to a condenser. The evaporator and condenser processes were modeled using Aspen Plus®. The parameters for the evaporation column were determined using vapor-liquid equilibrium data of *n*-hexane and water mixtures. The Non-random two-liquid model (NRTL) was used to generate such equilibrium data. The shell and tube model in Aspen Plus® was chosen to model the condenser.

2.4 Estimation of microbial capric acid MSP

The built-in cost models in the SuperPro Designer® were used to estimate the equipment costs of the seed and production fermentors, the RVF filter, and the solvent extraction column. The cost of the distillation column was estimated on the basis of the type of tray, the number of trays, and the tower diameter [29]. A cost correlation between purchase-cost and the outside surface area of the tubes was used to calculate the costs of the condenser, the reboiler, and other heat transfer equipment [30]. The purchase cost of the centrifuge was estimated using an empirical equation based on the diameter [30]. The equipment costs were updated to U.S. 2015 prices using chemical engineering plant cost indices. The ratio factors based on delivered equipment cost were used to estimate the fixed-capital investment for the capric acid production plant [29].

The required quantities of raw materials and utilities were calculated using the simulated material and energy balances. The prices of glucose, *n*-hexane, natural gas, and electricity were assumed as \$0.30 kg⁻¹, \$0.40 kg⁻¹, \$3.35 MMBtu⁻¹, and \$0.07 kWh⁻¹, respectively. The long term mean prices of electricity and natural gas were used in the calculation. These average values were estimated from the 2007-2015 data of electricity and natural gas prices in the U.S. [30,31].

The *n*-hexane price was obtained from the pure component database of SuperPro Designer®. The price of glucose was obtained from the managers of corn wet milling plants in the Midwest region of the U.S. (personal communication). Sugars can be made from various feedstocks, including lignocellulosic and corn. Currently, high capital costs and immaturity of the technology make the production of sugars from lignocellulosic feedstock economically unviable [32,33]. In addition, the use of impure lignocellulosic-derived sugars increases the downstream separation and purification costs of chemical production. We chose glucose derived from corn starch as a currently available, low cost feedstock suitable for capric acid production in North America.

A correlation between the plant capacity and the operating labor was used to determine labor charges [34]. The costs associated with maintenance and operating overheads were assumed as 8% and 23% of total purchased equipment cost and labor cost, respectively [34]. Wastewater treatment was assumed to take place in an external facility for a fee of \$0.22 per kg of organic material removed [34]. The calculations for the depreciation of capital investment were carried out using the Modified Accelerated Cost Recovery Systems (MACRS) method [34]. The general expenses were calculated as 10% of total revenues generated from the sales of capric acid [34]. An economic model was built using the estimated capital and operating costs. The discounted cash flow analysis method was used to estimate the MSP of capric acid [10]. A discount rate of 10% has chosen for this analysis [10]. The MSP of capric acid was calculated for various combinations of titers, yields, and volumetric productivities.

2.5 Estimation of GHG emissions and energy consumption

The GHG emissions and energy consumption of the process for the production of capric acid from glucose were estimated using the LCA approach. The functional unit was defined as 1

kg of capric acid made from corn. The system boundaries include cultivation of corn, conversion of corn to glucose through the corn wet milling process, and the microbial synthesis of capric acid from glucose.

The CO₂ emissions associated with corn grain production and the corn wet milling process to convert corn into glucose were obtained from Akiyama et al. [35] as 0.15 (kg) (kg glucose)⁻¹ and 0.35 (kg) (kg glucose)⁻¹, respectively. The value of CO₂ absorbed by corn plants from the air was accounted as 1.47 (kg) (kg glucose)⁻¹ [35]. This value was estimated from the stoichiometry of glucose formation by corn plants from water and CO₂. It requires a total of 7.5 MJ to make 1 kg of glucose from corn, which includes the energy requirements for corn planting, cultivating, harvesting, and wet milling [35]. The mass ratio allocation method was used to allocate process flows among the products of the corn wet milling process [35]. The electricity and steam requirements, which were estimated from the simulation of the process, were utilized to determine the energy consumption and GHG emissions associated with the production of capric acid from glucose. The lifecycle energy for producing 1 MJ of electricity and steam from natural gas in the U.S. and corresponding GHG emissions were found in the Ecoinvent database [36].

2.6 Estimation of selling price, GHG emissions, and energy consumption of coconut-oil-derived capric acid

A mixture of capric acid, octanoic acid, palmitic acid, and lauric acid and glycerol is formed when coconut oil is hydrolyzed [37]. The by-product glycerol is separated from the mixture of fatty acids using a distillation column [37]. The fatty acid mixture is then fractionated into capric, octanoic, palmitic, and lauric acids using fractional distillation column [37]. We did

not perform economic analysis of the conventional process for capric acid production, as the market price of capric acid is available from ICIS chemicals [38].

The environmental performance metrics of conventional production were estimated using the LCA approach. The functional unit was defined as 1 kg of capric acid made from coconut oil. The system boundaries include cultivation of coconuts, production of oil from coconuts, and the synthesis of capric acid from coconut oil. The life cycle inventories for processes of cultivation of coconuts and extraction of oil from coconuts were found in the Ecoinvent database [36]. The CO₂ uptake by coconut trees and the GHG emissions of the coconut oil production process were taken as 0.0097 (kg) (kg capric acid)⁻¹ and 0.23 (kg CO₂ eq.) (kg capric acid)⁻¹, respectively, for the calculation of the GHG emissions of the conventional process [36]. The GHG emissions of process for the production of capric acid from coconut oil were estimated as 0.29 (kg CO₂ eq.) (kg capric acid)⁻¹. This value was estimated using the process energy requirement of capric acid production from coconut oil. The material and energy balance data for hydrolysis, distillation, and fractionation processes were obtained from Gervajio [37]. The overall energy consumption and GHG emissions of the conventional process were allocated among capric, octanoic, palmitic, and lauric acids based on their concentrations in the fatty acid mixture.

3. Results

Since it is difficult to graph and visualize the multi dimensional performance surfaces that represent the effect of three or more variable process parameters on a performance metric, a three-dimensional representation is used. Based upon a personal communication from the Center for Biorenewable Chemicals (CBiRC) Scientific Advisory Board, a rule-of-thumb volumetric productivity target for a bulk chemical via microbial synthesis is 1-3 g l⁻¹ h⁻¹. The results of the economic analysis indicate that volumetric productivities greater than 2 g l⁻¹ h⁻¹ have a small

effect on the cost of capric acid production. For a given yield and titer, the production cost of making capric acid is reduced only by 5% when the volumetric productivity is increased from 2 g l⁻¹ h⁻¹ to 3 g l⁻¹ h⁻¹. The economic and environmental performance metrics of capric acid production are, therefore, estimated for a wide range of titers and yields and a constant volumetric productivity of 2 g l⁻¹ h⁻¹. The lower and upper bounds for yield and titer are assumed to be 10 and 100% of the maximum yield of capric acid and 10 and 200 g l⁻¹, respectively.

3.1 Energy, GHG, and cost performance surfaces

Performance surfaces for energy and GHG are generated by mapping energy consumption and GHG emissions to the corresponding titers and yields, respectively (Fig. 2a and Fig. 2b). The performance cost surface is created by plotting minimum selling prices on the z-axis and corresponding yields and titers on the x- and y-axes, respectively (Fig. 2c). For a given titer, the MSP, energy consumption, and GHG emissions of the capric acid production process are inversely related to yields (Fig. 2a, 2b, and 2c). In addition, the performance energy, GHG, and cost surfaces of capric acid production have a similar shape (Fig. 2a, 2b, and 2c). This indicates that the MSP, energy consumption, and GHG emissions of capric acid production are highly correlated. In other words, replacing corn with another feedstock, in an effort to reduce the total energy consumption of the process for capric acid production, will also increase or decrease the production cost.

A percentage change in the value of the yield will have a higher impact on performance metrics of capric acid production than the same percentage change in the value of the titer. For example, there is a nearly 500% increase in the total energy consumption as the capric acid fermentation yield drops from 0.38 g g⁻¹ to 0.04 g g⁻¹ for a given titer (Fig. 2a). On the other hand, for a given yield, there is only a 100% increase in energy consumption when the titer falls

from 200 g l⁻¹ to 20 g l⁻¹ (Fig. 2a). This is because any change in the value of the fermentation yield will have an effect on the entire upstream part of the capric acid production chain, including corn agriculture, glucose production from corn, and the fermentation processes.

When titers are low and yields are high, the variation in titer affects the energy consumption, GHG emissions, and MSP of the capric acid production process more than the yield does (Table 1). The energy consumption of the separation and purification processes dominates the overall energy consumption of the capric acid production process for low titers because of the high energy requirement to evaporate the large amount of water that is associated with low titers. Such a high energy requirement is the reason why low titers are associated with high production cost and high GHG emissions.

3.2 Energy, GHG, and cost feasible spaces

The cradle-to-gate energy consumption of the coconut-oil-derived capric acid production process is estimated as 49 MJ kg⁻¹, which is used to determine the constraint energy plane seen in Fig. 3a. The space between the energy performance surface and the constraint energy plane is referred to as the energy feasible space (Fig. 3a). We refer to the curve resulting from the intersection of the performance surface and the constraint plane as the feasible energy curve (Fig. 3a). For combinations of yield, titer, and volumetric productivity within the energy feasible space, the glucose-based capric acid production consumes an amount of energy that is less than or equal to that consumed in conventional capric acid production. This is because the use of a *E. coli* strain that can synthesize capric acid with a high selectivity avoids the requirement for the highly energy-intensive fractionation process that is used in the conventional process. In addition, the energy required to make glucose is less than that required to make coconut oil (data not shown).

The GHG space is created by determining the GHG constraint plane (Fig. 3b). The cradle-to-gate GHG emissions of conventional capric acid production are estimated as 0.51 (kg CO₂ eq.) (kg capric acid)⁻¹. The GHG emissions of the glucose-based capric acid production process are found to be negative for some combinations of process parameters (Fig. 3b). These negative emissions occur because the cradle-to-gate GHG emissions associated with capric acid production are less than the fixation of CO₂ into glucose by the growing corn plants. When capric acid is converted into products like fuel, the carbon stored in the capric acid is emitted as CO₂ during combustion. In such a case, the GHG emissions of the capric acid production process must be estimated without considering the value of CO₂ fixation as glucose.

The environmental impact of capric acid production will be low if the microorganism exhibits a high capric acid yield. This is because the formation of by-products significantly affects the GHG emissions of capric acid production. The minimum GHG emissions of -0.95 (kg CO₂ eq.) (kg capric acid)⁻¹ are determined for a fermentation titer of 200 g l⁻¹, a volumetric productivity of 2 g l⁻¹ h⁻¹, and a yield of 0.38 g g⁻¹ (Fig. 3b). The GHG emissions of capric acid production are increased to 34 kg CO₂ eq. when the yield drops to 0.04 g g⁻¹ (Fig. 3b). Such a large increase in the amount of GHG emitted is due to the formation of by-products. In this analysis, the by-product stream is assumed to be discharged as a waste sludge, and this sludge is treated at an external waste water treatment facility. The carbon present in the by-products can be oxidized to CO₂ and H₂O in the wastewater treatment plant using the aerobic digestion process [39].

The market price of capric acid is \$1.50 kg⁻¹ [38], which is used to determine the cost constraint plane (Fig. 3c). The space between the cost performance surface and the constraint cost plane is referred as the cost feasible space (Fig. 3c). The MSP of glucose-based capric acid

production is estimated over a range of process parameters following discounted cash flow analysis. A summary of capital and operating costs of the capric acid production plant is presented in Tables 2 and 3, respectively. The total capital investment and operating expenses for synthesizing capric acid vary with combinations of process parameters. The estimates in Tables 2 and 3 represent the capital and operating costs of synthesizing capric acid from glucose using a strain of *E. coli* that enables a titer of 75 g l⁻¹, a yield of 0.36 g g⁻¹, and a volumetric productivity of 2 g l⁻¹ h⁻¹. We will show subsequently that, for this yield, titer, and productivity, the microbial production system has a lower production cost than that of the conventional capric acid production process.

The risk to the capital investment associated with producing a biorenewable chemical is high when the market prices of the raw materials and the product are volatile [40]. In general, investors expect high return on investment (i.e. high profits) when there is a high investment risk. The cost feasible space shows obtainable profits with the production of capric acid using a biocatalyst for a wide range of process parameters (Fig. 3c). For a given investment risk, the cost feasible space can be utilized to determine titer, yield, and productivities that are necessary to generate the expected return on investment for the production of capric acid at a commercial scale. For example, if investors are expecting a profit of \$0.30 per kg capric acid when there is a high investment risk, it is necessary to develop a biocatalyst that produces capric acid at a yield of 0.38 g g⁻¹, a titer of 200 g l⁻¹, and a volumetric productivity of 2 g l⁻¹ h⁻¹ (Fig. 3c).

The feasible cost space can be used to guide the choice of a viable target molecule from the set of possible products that can be made from capric acid. For example, capric acid can be converted into 1-decanol via hydrogenation [37] and 1-nonene via decarbonylation [2]. The average market prices are \$2.20 kg⁻¹ for 1-decanol and \$1.50 kg⁻¹ for 1-nonene [38]. The cost

feasible space shows that a production cost of at least \$1.20 is necessary to synthesize one kg of capric acid from glucose (Fig. 3c). The feedstock (capric acid) contributions to the overall cost of 1-decanol and 1-decene production are \$1.32 kg⁻¹ and \$1.64 kg⁻¹, respectively. The feedstock cost contribution is estimated using practical yields that are based on conversion of capric acid. The margins left for energy and other operating costs of 1-decanol and 1-decene production are \$0.88 and -\$0.14, respectively, after subtracting the feedstock cost from the market prices of 1-decanol and 1-decene. Such a simple analysis indicates that the development of a technology for converting capric acid into 1-decanol is clearly a promising option. On the other hand, the negative margin indicates that development of a process for the production of 1-decene is economically unviable.

As shown in Fig. 3a, 3b, and 3c, the GHG feasible space is larger than the feasible spaces for energy and cost. In other words, there are more combinations of yield, titer, and productivity for which capric acid production meets the GHG constraint than there are combinations that meet the energy and cost constraints. However, capric acid production is considered to be economically and environmentally viable for a combination of process parameters only when the production meets all three constraints. In order to determine the combinations of process parameters that meet all three constraints, we define the two dimensional (2D) feasible space of capric acid production using energy, GHG, and cost feasible curves, the maximum biosynthesis pathway yield, the maximum assumed titer, and the fixed volumetric productivity.

3.3 2D-feasible space of the microbial capric acid process

The 2D-feasible space is defined for the glucose-based capric acid production by graphing the energy, GHG, and cost feasible curves in addition to the maximum yield and titer constraints (Fig. 4). The existence of a feasible space indicates that the glucose-based capric acid

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4 production process has the potential to meet or exceed the performance of the conventional
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6 process in terms of cost, energy consumption, and GHG emissions. If the graphing of feasible
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8 curves and constraints does not result in a feasible space, then the development of a biocatalytic
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10 technology must be stopped, in order to avoid unfruitful investments. This is because the lack of
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12 a feasible space indicates that the proposed biocatalytic route to capric acid cannot perform better
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14 than the conventional process.
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19 The feasible space in Fig. 4 can be used by a research and development team that is
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21 developing biocatalysts for synthesizing capric acid from glucose to find out whether the
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23 biocatalytic technology has attained the required economic feasibility and environmental
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25 sustainability. For example, the *E. coli* strain developed by the CBiRC research team currently
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27 exhibits a yield of 0.25 g g^{-1} , a volumetric productivity of $0.8 \text{ g l}^{-1} \text{ h}^{-1}$, and a titer of 15 g l^{-1} . The
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29 CBiRC research team has not yet achieved a process for the production of capric acid that is
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31 environmentally and economically feasible, as this combination of process performance
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33 parameters does not fall within the feasible space of capric acid production (Fig. 4). The
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35 economic and environmental viability of a capric acid production process requires further
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37 improvement of the biocatalyst. The feasible space of capric acid production can be used to set
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39 performance targets for further improvement of the biocatalyst.
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46 The trade-offs between yields and titers shown in Fig. 4 are used to set performance
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48 targets for the development team. The economic and environmental viability of capric acid
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50 production can be achieved through many different routes. For example, one route is to push the
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52 capric acid yields from 0.25 g g^{-1} to 0.38 g g^{-1} , the volumetric productivity from $0.8 \text{ g l}^{-1} \text{ h}^{-1}$ to 2 g
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54 $\text{l}^{-1} \text{ h}^{-1}$, and the titer from 15 g l^{-1} to 40 g l^{-1} (Fig. 4). Another route is to achieve titers of greater
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4 than 200 g l⁻¹ and a volumetric productivity of 2 g l⁻¹ h⁻¹, while maintaining a yield of 0.25 g g⁻¹
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6 (Fig. 4).
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9 The performance targets will be determined by identifying the best route from all
10 possible routes. The best route can be identified by comparing, among the possible routes, the
11 development time and costs that are necessary to achieve an economically and environmentally
12 viable process for capric acid production via each possible route. The research and management
13 teams can qualitatively estimate the development times and costs for each route. The
14 technological barriers and uncertainties that thwart attempts to improve fermentation yields,
15 titers, and volumetric productivities will impact the amount of time and money necessary for
16 achieving the performance targets. The resources necessary to push the performance level of a
17 biocatalyst will be high in the presence of technological barriers. Further research is necessary to
18 develop an analytic method or a framework that can be used to quantify the amount of time and
19 the cost required to push the currently attainable yields, titers, and productivities in order to meet
20 the performance targets.
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38 In addition to the trade-offs, the feasible space in Fig. 4 shows that there is a small effect
39 of increase in a capric acid titer greater than 100 g l⁻¹ on the MSP, GHG emissions, and energy
40 consumption of the process. Hence, the financial resources must be directed to improving
41 biocatalyst yields or production rates after the development team has managed to achieve a titer
42 of greater than 100 g l⁻¹ (Fig. 4). The results of feasible space analysis, therefore, can be utilized
43 to optimize the resources of time and money required for the development of the biocatalyst for
44 capric acid production.
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55 The fermentation metrics of at least 0.25 g g⁻¹ yield and 40 g l⁻¹ titer are desirable for
56 commercial relevance (Fig. 4). During scale up of capric acid production from laboratory- to
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4 pilot- and then to commercial scale, there is a possibility of performance loss, due to technical
5 risks [41]. For example, in the case of aerobic fermentations, difficulties in maintaining the
6 desired dissolved oxygen concentration in a commercial-scale fermentor could reduce the
7 performance levels of a microbial strain to values below those obtained in the laboratory-scale
8 fermentor. If such technical risks make it impossible to achieve biocatalyst yields of $\geq 0.25 \text{ g g}^{-1}$
9 or titers of $\geq 40 \text{ g l}^{-1}$, the development of a biocatalyst becomes unviable. In such a situation, it is
10 highly desirable to stop further development of the strain. There is no methodology in the
11 literature for quantifying such performance losses during the scale-up of a process for the
12 production of a biorenewable chemical. Experts in biomanufacturing, however, can estimate
13 such performance losses qualitatively from their experience of technology de-risking.
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28 Figure 4 shows that the feasible GHG and energy curves of capric acid production are
29 below the feasible cost curve. This indicates that capric acid production is environmentally
30 sustainable if it achieves economic viability, but the opposite may not be true. Since the cost of
31 the feedstock (glucose) dominates the overall production cost (Fig. S1), it may be possible to
32 shift the feasible cost curve to below the energy and GHG curves by developing a biocatalyst
33 that can synthesize capric acid from an inexpensive feedstock.
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43 Variation of the feasible space boundary in Fig. 4 can be caused by the price volatility of
44 glucose, natural gas, electricity, solvent, and capric acid [40]. Such a variation can be used to
45 indicate the financial risk associated with the investment for producing biorenewable chemicals:
46 there will be a low financial risk for producing capric acid if the variation of the feasible space
47 boundary of capric acid production is low. The variation of the feasible space boundary can be
48 quantified using a procedure based on Monte-Carlo simulation [42].
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58 **3.4 Sensitivity analysis**

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The feasible space in Fig. 4 shows how different values of titer and yield impact MSP, GHG emissions and the energy consumption of capric acid production. The feasible space analysis cannot show the impact that changes in a certain process assumption will have on the performance metrics of capric acid production. Thus, a sensitivity analysis is performed to identify process parameters that are key drivers of performance metrics of capric acid production. A fermentation yield of 0.36 g g^{-1} , a volumetric productivity of $2 \text{ g l}^{-1} \text{ h}^{-1}$, and a fermentation titer of 75 g l^{-1} are selected to perform the sensitivity analysis. The results of this analysis are also applicable to all feasible combinations of yields, titers, and volumetric productivities because we used the same assumptions when estimating the performance metrics of capric acid production over a range of process parameters.

The variation of the MSP is measured for a $\pm 10\%$ change in the prices of glucose, natural gas, and electricity, in the plant capacity, in the wastewater treatment cost, in the media cost, and in the fermentation turnaround time (Fig. S2). The results of the sensitivity analysis show that the MSP of capric acid is most sensitive to the glucose price. A 10% increase in the glucose price results in a 5% increase in the MSP of capric acid (Fig. S2). The plant capacity and the wastewater treatment cost have moderate impact on the capric acid MSP. A 3% decrease in the value of capric acid MSP is observed for a 10% increase in the value of plant capacity. The capric acid MSP is increased by 1% when the wastewater treatment cost per kg of organic material removed is increased from \$0.22 to \$0.24. The sensitivity analysis shows that the impact of natural gas and electricity prices on capric acid MSP is not significant (Fig. S2).

A variation in the values of CO_2 intake from air by corn plants is found when comparing the data of Weidema et al. [36] and Akiyama et al. [35]. The GHG emissions of steam and electricity generation vary with the type of fuel used for their production. Thus, the sensitivity of

GHG emissions associated with capric acid production is measured both for a $\pm 10\%$ change in the GHG emissions associated with the production of utilities and for a $\pm 10\%$ change in CO_2 intake (Fig. S3). A change in the value of CO_2 intake causes the most variation in the GHG emissions associated with capric acid production.

The sensitivity of overall energy consumption of capric acid production is measured for a $\pm 10\%$ change in the energy requirement values of the seed and production fermentations, and of the extraction, distillation, evaporation and glucose production processes. The process energy requirements of the fermentation and purification processes are considered in the analysis to determine the effect of uncertainties associated with the results of the Aspen Plus® and SuperPro Designer® process simulations. The energy required to make glucose from corn is the major parameter affecting the overall energy consumption (Fig S5). An 8% increase in the value of overall energy consumption results from a 10% increase in the value of the energy requirement of glucose production (Fig. S4).

4. Discussion

This work represents the first time that FSA, TEA, and LCA methods have been combined in the evaluation of a process for the production of a biorenewable chemical. In general, a single combination of process parameters is used while evaluating the economic and environmental performances of processes for the production of new biorenewable chemicals [3, 43-45]. For example, Efe et al. [3] assessed the economic viability of the succinic acid production process for a yield of $0.69 \text{ (g succinic acid) (g glucose)}^{-1}$, a specific productivity of $89 \text{ g kg}^{-1} \text{ h}^{-1}$, and a titer of 13.7 g l^{-1} . Under this combination of process parameters, the succinic acid production process is unviable, as the estimated MSP of succinic acid is greater than the market price of succinic acid. However, although the improvement of key process parameters

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4 might make this process viable, an analysis using a single combination of process parameters
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6 will not help to focus attention on the improvement of key process parameters.
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9   Patel et al. [6] reported a method to evaluate a new biobased process at an early
10 development stage. Their method considers only one process parameter, namely theoretical
11 yield, while assessing the environmental performance of the new biobased process against the
12 conventional chemical process. Such an assessment is not sufficient because the energy
13 consumption and GHG emissions of biocatalytic processes depend on the titer and the
14 volumetric productivity, along with the yield. Also, their method uses process costs and the
15 environmental impact (PCEI) index as a proxy for indicating overall production costs of a new
16 process for the production of a biorenewable chemical. The qualitative nature of the PCEI index
17 introduces uncertainty into the assessment of economic viability of the process.
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31   In this paper, we introduced a new approach by combining FSA, TEA, and LCA. This
32 combined analysis provides an alternative to the qualitative and the single-process-configuration
33 approaches for evaluating processes for the production of biorenewable chemicals. The feasible
34 space of a biorenewable chemical route can be defined in four steps. The first step is to create a
35 PFD for the production of the chemical. The second step consists of modeling the PFD to
36 estimate performance metrics (MSP, energy consumption, and GHG emissions) of the
37 production system for a wide range of process parameters. Performance surfaces for cost, energy,
38 and GHG are generated by plotting a performance metric on the z-axis and corresponding
39 process parameters on the x- and y-axes. The third step is to estimate the production cost, the
40 energy consumption, and the GHG emissions of the competing route. The performance metrics
41 of the competing route are then used to determine constraint planes for cost, energy, and GHG.
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58 The intersections between the performance surfaces for cost, energy, and GHG and the constraint
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planes for cost, energy, and GHG are used to produce the feasible cost, energy, and GHG boundaries, respectively. When these feasible curves are plotted, the area inside the boundaries defines the feasible space for the biorenewable chemical route in step 4.

The analysis of a biorenewable chemical process by combining FSA, TEA, and LCA analysis enables one to determine the process viability under all reasonable combinations of process parameters. If it is determined that the analyzed biorenewable chemical process is unviable for all combinations of process parameters, then further development of the process for the production of the new biorenewable chemical must be stopped to avoid probable losses of capital investments. The feasible space of a biorenewable chemical production process shows trade-offs among process parameters that can be used to set goals for the further development of the process. The feasible space of a chemical process is used to determine values of process parameters for which the investments for further improvement of a new biorenewable chemical process will result in insignificant economic and environmental benefits.

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Figure captions

Fig. 1. Proposed process for the production of capric acid from glucose.

Fig. 2. Performance surfaces of process for the production of capric acid from glucose (a) Energy performance surface (b) GHG performance surface and (c) Cost performance surface.

Fig. 3. Three-dimensional feasible space of process for the production of capric acid (a) Energy feasible space (b) GHG feasible space (c) and Cost feasible space.

Fig. 4. Two-dimensional feasible space for the production of capric acid from glucose bounded by titer, yield, and the cost curves for a constant volumetric productivity ($2 \text{ g l}^{-1} \text{ h}^{-1}$).

Tables

Table 1

Dominant process sections of capric acid production.

	Region 1 ^[a]	Region 2 ^[b]	Region 3 ^[c]	Region 4 ^[d]
Feedstock (Glucose) production				
Seed fermentation				
Product fermentation				
Separation and purification				

The performance surface is used to identify process sections that dominate the overall performance of capric acid production. In order to find dominant process components, we divide the performance surface into four regions.

^[a] Region 1 represents high titers ($>100 \text{ g l}^{-1}$) and high yields ($>0.32 \text{ g g}^{-1}$) region of the performance surface;

^[b] Region 2 represents the high titers ($>100 \text{ g l}^{-1}$) and low yields ($<0.16 \text{ g g}^{-1}$ & $>0.04 \text{ g g}^{-1}$) region of the performance surface;

^[c] Region 3 represents the low titers ($<30 \text{ g l}^{-1}$ & $>10 \text{ g l}^{-1}$) and high yields ($>0.32 \text{ g g}^{-1}$) region of the performance surface, and

^[d] Region 4 represents the low titers ($<30 \text{ g l}^{-1}$ & $>10 \text{ g l}^{-1}$) and low yields ($<0.16 \text{ g g}^{-1}$ & $>0.04 \text{ g g}^{-1}$) region of the performance surface.

Black shading indicates the dominant process section in a particular region of the energy performance surface

Thick grey shading indicates the dominant process section in a particular region of the GHG emissions performance surface

Light grey shading indicates the dominant process section in a particular region of the cost performance surface

Table 2

Components of total capital investment for capric acid production.

Million U.S. Dollars 2015	
Total equipment purchase cost (TEP)	7.0
Installation cost (39% of TEP)	2.7
Instrumentation (43% of TEP)	3.0
Piping (31% of TEP)	2.1
Electrical (10% of TEP)	0.7
Buildings (15% of TEP)	1.05
Yard improvements (12% of TEP)	0.84
Service facilities (55 % of TEP)	3.8
Total direct plant costs (TDC)	21.4
<i>Indirect costs</i>	
Engineering & Supervision (32% of TEP)	2.24
Home office & Construction (34% of TEP)	2.38
Contingency (15% of TEP)	1.05
Legal expenses (4% of TEP)	0.28
Contractors fee (19% of TEP)	1.33
Total indirect capital costs (TIC)	7.28
Working capital (5% of TDC+TIC)	1.43
Solvent cost	0.031
Total capital investment ^[a]	30.1

^[a]This estimated capital investment is for synthesizing capric acid via microbial technology that has achieved fermentation yields of 0.36 g g⁻¹, volumetric productivity of 2 g l⁻¹ h⁻¹, and fermentation titer of 75 g l⁻¹

Table 3

Operating expenses for capric acid production from glucose.

Million U.S. Dollars 2015	
Glucose	10.7
Media	0.9
Utilities	1.7
<i>n</i> -Hexane (make-up solvent)	≈0
Waste disposal	0.25
Fixed costs ^[a]	2.9

^[a] Fixed costs include labor wages, property taxes, insurance, operating overhead, and depreciation
These estimated operating expenses are for synthesizing capric acid via microbial technology that has achieved fermentation yields of 0.36 g g⁻¹, volumetric productivity of 2 g l⁻¹ h⁻¹, and fermentation titer of 75 g l⁻¹

Figure 1

Figure 2

Figure 3

Figure 4