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Large-Scale Fermentation of E. Coli for the Production of High-Purity Isoprene

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Large-Scale Fermentation of E. Coli for the Production of High-Purity Isoprene

Abstract
We present a process for the production of isoprene via the fermentation of glucose. Based on our current specifications, we conclude that the use of recombinant E.coli for the fermentation of glucose is a novel yet unprofitable venture. Our current design entails the continuous production of isoprene using 3 pre-seed, 3 seed, and 5 production fermenters each with a production fermentation time of 72 hours. Our scheduling of the fermenters allowed us to produce isoprene continuously at a steady rate, and the liquid by-products of the fermentation were removed and sterilized at the end of each batch. Isoprene was mainly present in the vapor phase during the fermentation and was purified using a combination of an absorption using ISOPAR v, stripping with steam, and separation using a flash vessel.

It was desired that the fermentation was operated near the minimum oxygen concentration (MOC) as such conditions allowed for the highest production rate of isoprene based on the preliminary studies done by Chotani in their patent. The fermentation was operated at 34 °C and 1.7 bar with glucose and oxygen as the reactants producing isoprene, carbon dioxide, and water as the products.

The results of our design suggest that the price of isoprene is too low when compared to the costs of raw materials, making this process economically unfeasible under present market conditions. We project that $4.08 worth of glucose will be need for each pound of isoprene which currently goes for $0.79/lb. Additionally, the metabolic pathway of isoprene is highly exothermic, requiring large utility requirements in terms of chilled water to remove heat from the fermenters. We are unsure of impacts of rapidly changing the temperature of E.Coli on production as there is no data regarding the robustness of the strain. Overall, the fixed capitals costs incurred make this process even more unappealing for further consideration.

Disciplines
Biochemical and Biomolecular Engineering | Chemical Engineering | Engineering

April 12th, 2016

Dear Dr. Fabiano, Dr. Bockrath and Dr. Bidstrup-Allen,

Our team submits the following design proposal for the project of using a fermentation process for the production of isoprene. We thank you for your continued guidance over the semester in completion of this design.

The following design used hand calculations to make the initial estimates for the equipment sizes and material balances. Aspen v8.8 was use to take these initial estimates and fine tune various parameters required in the process to close the loops to recycle and conserve materials. Since Aspen does not handle batch processes well, the key processes involving the fermenters were designed with the aid of Excel.

While the overall plant design is complete, external market forecasts are a significant factor for making the managerial decision to pursue this joint venture. We project that this design will not become profitable unless industry conditions drastically change the price of glucose or isoprene. Isoprene prices are too low as a commodity chemical to justify the use of a biological process at this time.

Sincerely,
Phillip Taylor
Yuta Inaba
Ian Pinto

Large-scale Fermentation of E.coli for the Production of High-Purity Isoprene

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Abstract

We present a process for the production of isoprene via the fermentation of glucose. Based on our current specifications, we conclude that the use of recombinant E.coli for the fermentation of glucose is a novel yet unprofitable venture. Our current design entails the continuous production of isoprene using 3 pre-seed, 3 seed, and 5 production fermenters each with a production fermentation time of 72 hours. Our scheduling of the fermenters allowed us to produce isoprene continuously at a steady rate, and the liquid by-products of the fermentation were removed and sterilized at the end of each batch. Isoprene was mainly present in the vapor phase during the fermentation and was purified using a combination of an absorption using ISOPAR v, stripping with steam, and separation using a flash vessel.

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The results of our design suggest that the price of isoprene is too low when compared to the costs of raw materials, making this process economically unfeasible under present market conditions. We project that \$4.08 worth of glucose will be need for each pound of isoprene which currently goes for \$0.79/lb. Additionally, the metabolic pathway of isoprene is highly exothermic, requiring large utility requirements in terms of chilled water to remove heat from the fermenters. We are unsure of impacts of rapidly changing the temperature of E.Coli on production as there is no data regarding the robustness of the strain. Overall, the fixed capitals costs incurred make this process even more unappealing for further consideration.

Introduction and Objective Time Chart

This design project originates from analyzing whether the Dupont/Goodyear joint venture to manufacture isoprene using the fermentation of sugar is a viable approach to compete with traditional petrochemical manufacturing processes. A plant design using this process will be detailed to see whether this process is economically viable for these companies.

Table 1 displays the initial charter for this project addressing the breadth and depth of the analysis presented.

Table 1: Project Charter

Project Name: Isoprene production from fermentation of E.Coli on sugar
Specific Goals: Design a plant for this process at an industrial-scale for economic analysis
Project Scope: In-scope • Using patented information as estimates of the production rates and production platform • Evaluating different design alternatives to minimize cost while maintaining feasibility • Evaluate profitability of the process or lack thereof and find the most significant factors that affect the viability of the process Out-of-scope • Attempting to propose other platforms and methods to biologically produce isoprene

• Proposing new technologies that have not been used industrially within reasonable assumptions
Deliverables: • Plant design for fermentation process • Projected equipment specifications • Assessment of plant/market economics
Time Line: Design completed over 3 months

Market and Competitive Analysis

Since January 2012, the U.S. import price for isoprene has been pushed downwards from prices upwards of the $3500/ton range to prices around $1500/ton in mid-2015. The price of isoprene is generally bounded by the price of rubber. The price of rubber (RSS3 grade) peaked in early 2011 at roughly $2.70/lb of rubber. The increased production of natural rubber in Asia has oversupplied the market and currently remains at $0.70/lb (Figure 1). On top of increased supply of natural rubber, the demand for rubber has fallen as China's historically strong growth slowed. With China's economy expanding much more slowly, consumption of rubber and isoprene will not see much growth until 2020 as the market readjusts for the excess inventories of rubber[1].

Figure 1. Monthly rubber prices per pound

As for the market for isoprene monomer in North America outside of synthetic rubber, a majority of imported isoprene is polymerized to form adhesives. While imports have increased

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[1] http://www.bloomberg.com/news/articles/2015-03-23/world-rubber-demand-slowdown-seen-weighing-on-price-through-2020

significantly since 2008, many businesses are choosing to buy isoprene from markets where rubber prices have influenced isoprene spot sales.

The price for natural rubber remains a fairly good estimate for high-purity isoprene to be produced in this process as 70% of isoprene was polymerized for end-use in tires in 2013[2]. Therefore, natural rubber prices must recover for isoprene prices to increase again. Furthermore, isoprene is currently produced as a byproduct of catalytic cracking in petrochemical processes. With low crude oil prices forecasted over the next several year, isoprene will remain relatively cheap to produce using traditional approaches. Roughly 800,000 tons of petrochemical isoprene is polymerized to cis-polyisoprene each year.

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[2] https://www.ihs.com/products/isoprene-chemical-economics-handbook.html

Preliminary Process Synthesis

The production of isoprene via fermentation requires a minimum oxygen concentration (MOC) of 9.97%. During the early stages of the process synthesis, there were two flow sheets which satisfied this requirements.

Option A: Air can be used as the source of oxygen and N_2 gas can be used as a diluent.

Option B: The fermenter-off gases can be recycled and mixed with air so that the MOC is satisfied.

The objective was to operate the fermentation near the MOC since it allowed for the highest rate of production of isoprene as referenced by one of our patents, US 2011/0178261 (2.2 g/hr-L).

1. Use of Nitrogen Gas as a Diluent

The reaction pathways for both Options A and B were the same. The nitrogen gas would have to be obtained from a cryogenic plant and this option was ruled out due to the large volumes of nitrogen gas that would be required for the dilution. The alternative—i.e. option B—was determined to be favorable since it did not require the use of a diluent. Assuming the N_2 flow rate assumed below, 31,531,130 SCFH of nitrogen flow would be required. From Airgas' website, a Cryo-turbine plant would have a maximum capacity of 400,000 SCFH[3]. To meet our diluent requirements, 8 cyroplants would be required to supply enough air. These plants would

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[3] https://www.airgas.com/medias/305-On-Site-Nitrogen-System-Services.pdf?context=bWFzdGVyfHJvb3R8NzA2Njg1fGFwcGxpY2F0aW9uL3BkZnxoMmMvaDI1LzkwNzY5MjcyMDEzMTAucGRmfGMzYjI1YWM1Zjc5ZWUyZmZiMzRjOWRlNDM5NmU2YTE1Y2JmNmE3NWY3MTdhY2VjYmNlODA4ZmUyZTc5NmNjMWE

also incur heavy land costs and operating expenses as well as a large fixed capital investment. Therefore, this option was not pursued any further.

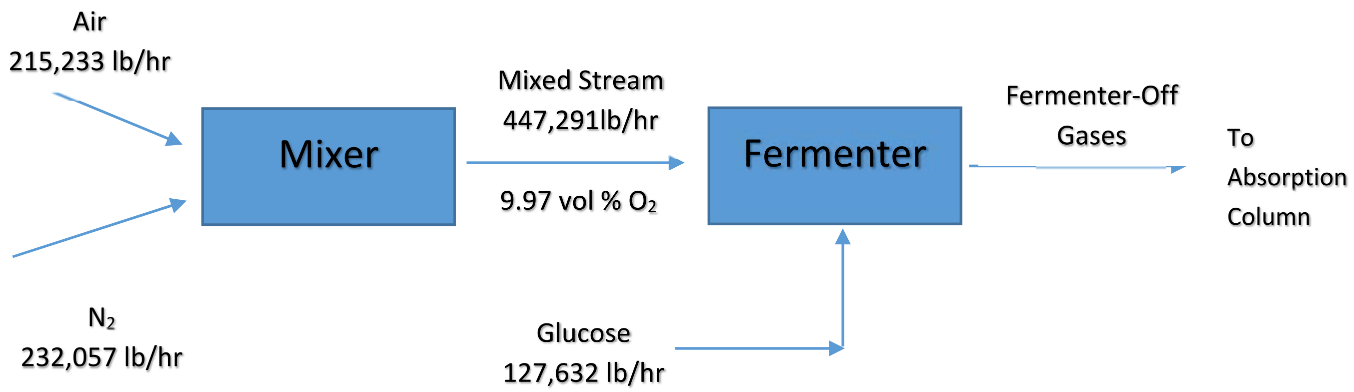


Figure 2.1 *Unit operations for the dilution of air with N_2 gas (Option A)*

2. Recycling of the Fermenter-off Gases

Option B involves the recycling of the fermenter-off gases. The fermenter off gases first enter an absorption column where the isoprene is absorbed from the gas phase. The remaining gas components which are mainly incondensable gases then leave the absorption column. This gas stream is split to purge some of the gases and the remainder is mixed with the air stream to be fed to the fermenter.

It is also important to note that a fraction of the vapor stream that is leaving the absorption column has to be purged. There are several inerts in the process such as nitrogen and argon. To avoid any accumulation of these inerts in the system, a fraction of the vapor stream has to be purged before it's mixed with the feed gas.

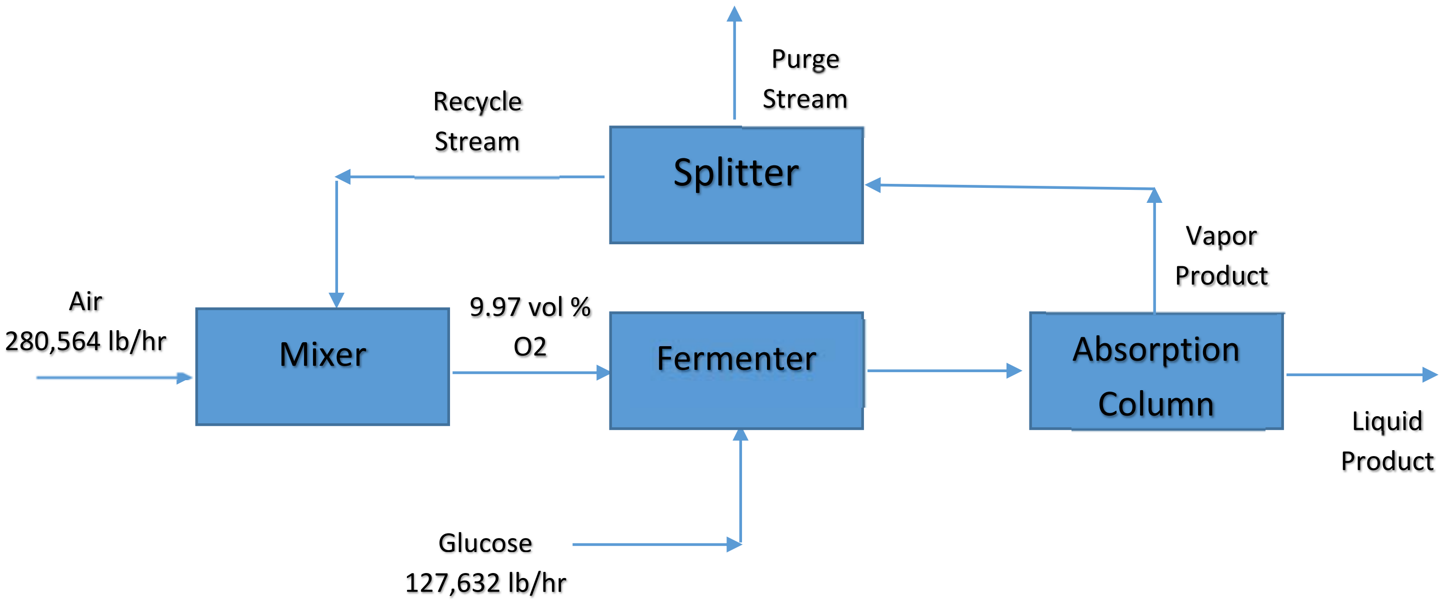


Figure 2.2 *Unit operations for the dilution of air by recycling the fermenter-off gases (Option B)*

Assembly of Database

The heat capacities, boiling points, molecular weights, and toxicity data were obtained for all of the components as the relevant thermophysical properties in the process. Based on the results of US 2011/0178261, the isoprene producing strain CMP1043 of E.coli will produce isoprene at the following rate with the reaction:

Rate of isoprene production = 2.2 g/hr-L (where L represents per L of broth volume) using the pathway,

$C_6H_{12}O_6 + 3.41\ O_2 = 0.370\ C_5H_8 + 4.15\ CO_2 + 4.52\ H_2O$.

Table 2: Thermophysical Properties, Toxicity, and Price of Principal Chemicals

Component	*C_p at 25°C (J mol^{-1} K^{-1})*	*Boiling Point (°C)*	*MW (g/mol)*	*Price (per lb)*
Isoprene	144.75	34	68.12	$0.79
Oxygen	29.10	-183	16	N/A
Glucose	218.6	410.8	180.16	$0.40
Carbon Dioxide	29.10	-78.5	44.01	N/A
Water	4184	100	18.02	$0.20/$m^3$
Nitrogen	29.10	-195.8	14.01	N/A
Argon	20.79	-185.8	39.95	N/A
Isopar				$0.64

Note: Any prices which were listed as N/A were not used in the profitability analysis. These components were either by-products (for example, water) or were raw materials that were obtained from ambient air.

The by-products could not be sold due to their low purities and thus they were excluded from the profitability analysis. We also assumed the extracellular production of other compounds were minimal using a biological pathway. Also, the heat capacities for oxygen, carbon dioxide, nitrogen, and argon were computed assuming ideal gas behavior.

Process Flow Diagram and Material Balance

Our process flow diagram and a break-down of stream properties within the process is show below.

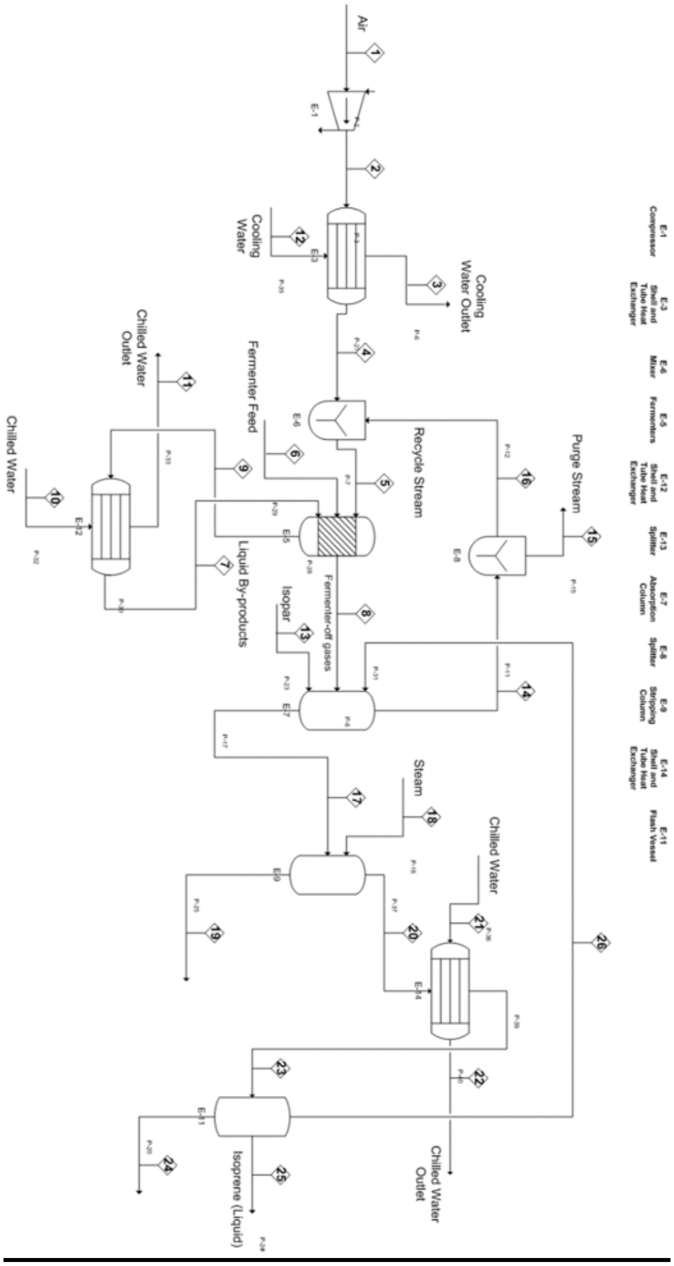


Figure 3. Process Flow Diagram

Table 3.1. Material Balance Block

Stream Number	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***
Temperature (°C)	25	90.85	80	34	34.09	34	25	34	34	5
Pressure (bar)	1.01	1.7	1.01	1.7	1.7	1.7	1.7	1.7	1.7	1.01
Vapor fraction	1	1	0	1	1	0	0	1	0	0
Mass flow (lb/hr)	280,565	280,565	58,731.2	280,565	623,543	127,632	8,893,900	678,632	8,893,900	23,796,890
Molar flow (lbmol/hr)	9686.67	9686.67	3260.07	9686.67	20705.49	2621.31	493,550	21,597	493,550	1,320,875.34
Component molar flow: (lbmol/hr)										
Isoprene	0	0	0	0	2.01	0	1.46	185.5	1.46	0
Oxygen	2029.4	2029.36	0	2029.3	2388.6	0	0.54	697.5	0.54	0
Glucose	0	0	0	0	0	495.91	0	0	0	0
Carbon Dioxide	2.62	2.62	0	2.6154	2187.4	0	78.78	4244.81	78.78	0
Water	0	0	3260.07	0	343.9	2125.399	493,462.97	685.74	493,462.97	1,320,875.34
Nitrogen	7564.32	7564.32	0	7564.32	15596.4	0	6.29	15596.34	6.29	0
Argon	90.38	90.3766	0	90.3766	186.3	0	0.16	186.34	0.16	0
Isopar	0	0	0	0	0.863	0	0.01	0.864	0.01	0

Stream Number	***11***	***12***	***13***	***14***	***15***	***16***	***17***	***18***	***19***	***20***
Temperature (°C)	15	30	34	34.18	34.18	34.18	34.85	115.61	107.75	98.39
Pressure (bar)	1.01	1.01	1.7	1.7	1.7	1.7	1.7	1.7	1.7	1.7
Vapor fraction	0	0	0	1	1	1	0	1	0	1
Mass flow (lb/hr)	23,796,890	58,731.2	3,373,580	665,975	322,998	342,977	3,391,740	337,594	3,693,380	35962.34
Molar flow (lbmol/hr)	1,320,875.34	3260.07	18298.37	21395.76	10376.94	11018.81	18616.27	18739.29	36128.68	1226.881
Component molar flow: (lbmol/hr)										
Isoprene	0	0	0	3.90	1.89	2.01	215.25	0	3.83E-18	215.25
Oxygen	0	0	0	697.49	338.28	359.21	1.566	0	5.97E-48	1.566
Glucose	0	0	0	0	0	0	0	0	0	0
Carbon Dioxide	0	0	0	4242.27	2057.50	2184.77	57.944	0	1.93E-29	57.94
Water	1,320,875.34	3260.07	0	667.85	323.90	343.94	19.089	18739.29	17838.89	919.49
Nitrogen	0	0	0	15596.23	7564.17	8032.06	24.324	0	3.91E-50	24.32
Argon	0	0	0	186.33	90.37	95.96	0.542	0	3.62E-50	0.542
Isopar	0	0	18298.37	1.677	0.813	0.864	18297.55	0	18289.79	7.765

Table 3.2. Material Balance Block

Stream Number	***21***	***22***	***23***	***24***	***25***	***26***
Temperature (°C)	5	85	15	15	15	15
Pressure (bar)	1.01	1.7	1.7	1.7	1.7	1.7
Vapor fraction	0	1	0.25	0	0	1
Mass flow (lb/hr)	136,657	136,657	35962.34	16577.05	13882.16	5503.329
Molar flow (lbmol/hr)	7592.06	7592.06	1226.881	918.9713	191.3231	116.591
Component molar flow: (lbmol/hr)						
Isoprene	0	0	215.25	0.121	181.46	33.665
Oxygen	0	0	1.566	0.000571	0.00835	1.557
Glucose	0	0	0	0	0	0
Carbon Dioxide	0	0	57.94	0.591	1.942	55.4117
Water	7592.06	7592.06	919.49	918.25	0.0376	1.197
Nitrogen	0	0	24.32	0.0044	0.0999	24.221
Argon	0	0	0.542	0.0002162	0.0047	0.537
Isopar	0	0	7.765	4.833E-06	7.765	7.17E-05

Process Description

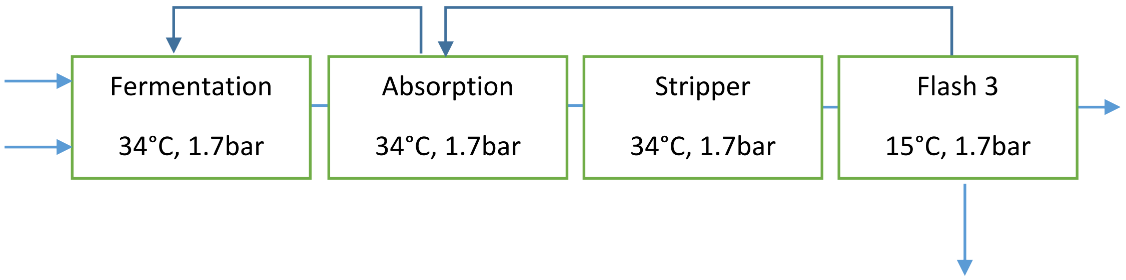


Figure 4. Block Flow Diagram for Isoprene Fermentation Process

5. Process overview:

The fermentation process is carried out using E.coli as a host platform. Once E.coli is grown to the necessary concentrations, the isoprene production pathway is induced with isopropyl-beta-D-1-thiogalactopyranoside (IPTG). Once induced, we assume that growth stops and all glucose consumption by the microbe is directed towards the pathway. The off-gas from the fermenter is taken off, carrying nearly all of the isoprene produced and sent to the absorption column. In the absorption column, the fermenter off-gas is contacted with ISOPAR V, modeled as a C13 paraffin solution in ASPEN, to bring the isoprene into solution. The remaining incondensable gases are recycled back to the fermenter to bring the feed gas to 9.97% O_2 to be outside of the flammable levels for isoprene.

The isoprene-rich Isopar is piped to the stripper column where steam is injected to vaporize the isoprene back into vapor phase for separation from Isopar. The steam stream carrying the isoprene vapor enters a 3-phase flash at 15°C where more of the inert gases are returned to the absorption column for further removal of isoprene. The two liquid phases exiting the flash vessel are a water stream and a liquid isoprene stream containing some Isopar contaminant. The isoprene stream is purified to 95% where it is stored at a quality grade that can be used for polymerization. 0.02% wt% tert-butylcatechol is added to the isoprene to prevent polymerization before usage.

2. Process Details:

The compressor (Block E-1) is used to bring the feed gas from the atmosphere up to 1.7 bars which is the pressure used in the fermentation process. This pressure was chosen because it was the pressure tested at the bench-scale in the patents for the production of isoprene. Although other pressures could most likely be used, there was no data to justify a use of a higher pressure. Furthermore, a higher backpressure in the fermenters would allow for greater removal of isoprene from the fermenter batch liquid rather than piping in gases at atmospheric pressure.

The mixer (Block E-6) at the beginning of the process is used to lower the feed gas O_2 concentration down to 9.97%. During the patent review, it was discovered that the E.Coli was consistently grown in reduced oxygen levels. Reduced oxygen helped drive carbon flux towards the isoprene production pathway in E.Coli. 9.97% O_2 in the feed gas was specifically chosen to maximize the rate of production and reduce the risks of creating a flammable mix of vapors. From the patent data, higher oxygen concentrations would lower the productivity of E.Coli. The mixer combines air from the atmosphere as a source of O_2 and the incondensable gases from the absorption column (Block E-7) because using a N_2 diluent source from an air liquefaction plant or membranes is costly when only the oxygen concentration is the only important factor within the feed gas as mentioned in the preliminary process synthesis.

The fermenters (Block E-5) are not well-represented in the flow diagram. The production of isoprene calls for a continuous process for efficient purification to create the final product.

However, fermenters are typically not run continuously because of the increased risk of contamination as time goes on; running fermenters in batch will allow for better response to contaminated tanks as those cultures would need to be restarted. Our process proposes a 3-stage step-up process from the shaker flasks produced in the laboratory to the full-scale fermentation tanks used for isoprene production. From the 500mL shaker flasks grown from the initial stocks of recombinant E.Coli, the pre-seed fermenters will grow the E.Coli up to 5L at 15g/L concentration, taking 16 hours with exponential growth. The contents of the pre-seed fermenters will be transferred into the seed fermenters to grow the E.Coli up to 88 m^3 at 15g/L concentration, taking another 26 hours with exponential growth. Once the E.Coli enters the fermenters for production, each fermenter will be in growth phase for 8 hours to bring the bacteria to 880 m^3 at 15g/L where it will be ready to be induced using IPTG for directing glucose consumption to the isoprene production pathway.

The process requires 4 production fermenters to produce a fixed amount of isoprene per hour for continuous downstream processing assuming an 8 hour growth phase, 72 hour fermentation phase, 10 hours for CIP/SIP, and 2 hours before the start of another batch to feed in all the starting materials. However, this number is highly optimistic as we expect some batches to become contaminated with other bacteria over the fermentation process, requiring a shutdown of these fermenters. As such we propose to have an extra fermenter that will continually be in the growth phase, ready to be induced for isoprene production in case any of the other fermenters need to be taken off-line prematurely before the end of the batch cycle. Figure 5 shows a sample Gantt chart of how the fermenters, seed fermenters, and pre-seed fermenters should be scheduled to ensure a stable production rate. In this design, 5 fermenters, 3 seed fermenters, and 3 pre-seed fermenters were used, but extra capacity for all fermenters should be considered if the engineered E.Coli is weak, where there is a high probability of the cell culture dying out. At the operating temperature and pressure of 34°C and 1.7 bar, isoprene is at a sufficiently dilute concentration that all of the isoprene is vaporized into the off-gas.

Additionally, the seed and pre-seed fermenters will be designed to run at atmospheric pressure. These fermenters will operate closely to a purely batch fermenter as all nutrients, mainly glucose will be charged to the fermenters before the addition of E.Coli. However, to promote the mass transfer of oxygen into the media, an arbitrary amount of filtered air will be pumped through the fermenter so that oxygen can dissolve into the liquid as it is agitated. Although 2.24 moles of oxygen is need for every mole of glucose consumed, any flow rate higher than the stoichiometric amount can be used for equipment convenience. Once the E.Coli is grown up to the amounts necessary for seeding the production fermenters, the liquid will be pumped to a pressure of 1.7 bar before it is added.

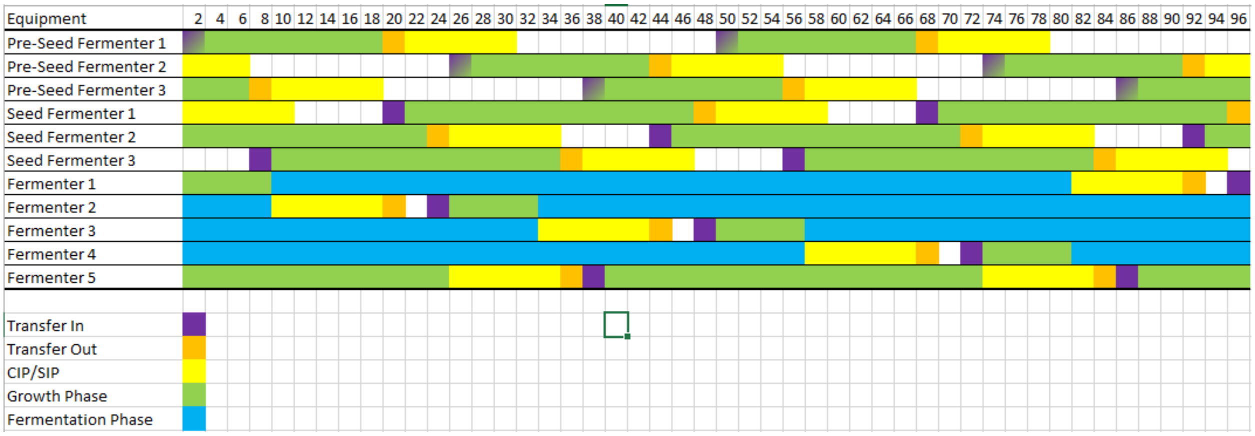


Figure 5. Fermenter Scheduling

The off-gas from the fermenter is taken to the absorption column (Block E-7) where it is contacted with Isopar v to bring the isoprene back into the liquid phase. The process is designed so that nearly all of the isoprene is moved into the Isopar so that the only gases leaving the absorption column are incondensable inerts and water vapor. The vapors leave the top of the column at 34.8°C while the bottoms leave at 34.2°C

The isoprene-rich Isopar stream is injected into the stripping column (Block E-9) along with saturated steam at 1.7 bar to vaporize the isoprene one more to separate the Isopar and isoprene. The isoprene leaves the stripping column with the remaining steam and incondensable gases at 107.8°C while the Isopar leaves at the bottom of the column with a second water phase at 98.8°C. The bottoms from the stripping column which contains roughly a 50:50 split of water and Isopar can be decanted to send the Isopar back to the absorption column so that the Isopar does not need to be continuously replaced except for the small amount that is vaporized by the steam and leaves the stripping column through the top.

The high temperature vapor stream carrying the isoprene is then cooled in a heat exchanger (Block E-14) with chilled water to bring the temperature of the stream down to 15°C. A 3-phase flash system (Block E-11) is used to separate the inerts, water, and isoprene/Isopar into different streams. A distillation column was considered as an alternative to the flash system, but the flash system was able to reach a high purity of isoprene without having to use additional theoretical stages. Since a chilled water system is needed for the cooling the fermenters, the benefits of adding a small amount of additional chilled water to the system for cooling the vapor stream outweighs the costs associated with manufacturing and operating a distillation column. The inerts that leave from the top of the flash is recycled back to the absorption to give a chance for the Isopar to be separated again, while the water can be collected for use in the fermenters again.

Energy Balance and Utility Requirements

This process requires a large amount of chilled water to cool the fermenters in production. From the heat of formation calculations, the production of isoprene releases 1636 kJ/mol of glucose consumed. To meet our production needs, 451,193,000 kJ/hr of heat is released by the 3 production fermenters. While it was desirable to meet the heat removal requirements by using a combination of heat jackets and internal cooling loops, our calculations showed that it would not be possible to fit enough tubes within the fermenter to allow for enough surface area contact. Therefore, the fermenter contents will be pumped to an external heat exchanger (Block E-12) to remove excess heat using chilled water. This will assume that any increase in temperature experience before the heat exchanger will not affect the E.Coli. Since chilled water cannot be heat beyond 15°C before returning it to the cooling tower, the chilled water is a self-contained loop. Some additional chilled water will be needed for the vapor stream leaving the stripping column to cool it down to 15°C before it enters the flash vessel for the separation of isoprene from the other gases and water.

The compressed air introduced for the feed gas and the vapor stream leaving the stripping column will also need cooling. Since the temperatures of this stream is 90.9°C cooling water can be used as the cold stream for the heat exchanger cooling the air stream (Block E-3). For the pre-flash heat exchanger (Block E-14), since the required temperature is 15°C, chilled water will need to be used for this heat exchanger as well.

Many process requires the removal of heat because the process is constantly generating heat through fermentation and steam is added at different places to aid with separation of our product. As such, there is a high demand for cooling, while we do not see the need for much heating within the process. Therefore, there is minimal benefits gained by attempting to integrate the heat exchanger network, and so each heat exchanger is standalone. The following table describes the cooling demands for various streams within the process.

Table 4. Cooling demands within process

Cooling Requirement	From	Change in T	To	Change in T
$4.512*10^8$ KJ/hr	Stream 9	34°C to 25°C	Stream 10	5°C to 15°C
$7.238*10^6$ KJ/hr	Stream 2	90.9°C to 34°C	Stream 12	30°C to 80°C
$2.075*10^7$ KJ/hr	Stream 20	98.4°C to 15°C	Stream 21	5°C to 85°C

Equipment List and Unit Descriptions

1. Absorption Column.

The absorption column (Block E-7) was designed using a combination of hand calculations and Aspen simulations. The number of actual stages that were required for the separation was estimated using the Kremser equation. The calculations of the absorption factor and number of actual stages are shown in the appendix.

Since the number of stages is an input for the Aspen flow sheet, the material balances for the system were first solved by hand and the resulting flow rates were used for the Kremser calculations. Also, Raoult's law was used to calculate the K-value of isoprene assuming the feed stream to the absorption was behaving ideally. Raoult's law assumes an ideal mixture so the Kremser calculations were based on this assumption. The number of actual stages was determined to be *20 stages* and sieve trays were used.

The diameter and height of the column were estimated using two methods: (1) using hand calculations in Microsoft Excel, and (2) using Aspen simulations. After the number of stages was computed using the Kremser method, the value was inputted into Aspen and the flow rates of the absorption's column feed stream, the column's vapor product, and liquid product were obtained from the simulation. These values were used to perform a flooding velocity calculation which was then used to estimate the diameter and height of the column using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo.

The value for the diameter of the column was compared to the value that was obtained from Aspen's Tray Spacing Report. It's important to note that Aspen's estimate for the column diameter was used for the calculations of the column's capital and operating costs. The diameter of the column was determined to be *34.81 ft* with a height of *54 ft***.** Carbon Steel (SA-285 Grade C) was chosen as the material for column due its price and availability and the sieve trays were also made of Carbon Steel (SA-285 Grade C).

Using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo, the thickness and weight of the column were estimated, using the operating pressure of 1.7 bar. The weight was then used to determine the vessel cost and the purchase costs of the 20 sieve trays were also computed. The bare-module factor for the column was determined to be 4.16 with a total bare-module cost of *$18,608,456***.**

Since this is an absorption column, there is no reboiler or condenser. The only operating cost stems from the use of Isopar as a solvent for isoprene. The operating costs were determined to be *$2,159,091*.

When modeling the absorption column in ASPEN, the convergence of the column was highly sensitive to the flow of Isopar. The Isopar flow had to be gradually reduced to find the minimum flow rate that achieved our separation requirements. Carbon steel was used as the construction material due to its low costs and mild operating conditions. Design calculation initially done by hand can be found in the Appendix, and the specification sheet can be located on page 38.

2. Stripping Column

The stripping column was designed using a similar method to that of the absorption column. The stripping column (Block E-9) was designed using a combination of hand calculations and Aspen simulations. The number of actual stages that were required for the separation was estimated using the Kremser equation and the detailed calculations are shown in the appendix.

As was mentioned in the previous section, the material balances for the system were first solved by hand and the resulting flow rates were used for the Kremser equation calculations. Raoult’s was used to calculate the K-value of isoprene assuming the feed stream to the absorption was behaving ideally. The number of actual stages was determined to be *20 stages* and sieve trays were used.

The diameter and height of the column were estimated using two methods: (1) using hand calculations in Microsoft Excel, and (2) using Aspen simulations. After the number of stages were computed using the Kremser method, the number of stages was inputted into Aspen and the flow rates of the stripping’s column feed stream, the column’s vapor product, and liquid product were obtained from the simulation. These values were used to perform a flooding velocity calculation which was then used to estimate the diameter and height of the column using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo.

The value for the diameter of the column was compared to the value that was obtained from Aspen’s Tray Spacing Report and the values that were generated by Aspen were used for the estimates of the column’s capital and operating costs. The diameter of the column was determined to be *39.5 ft* with a height of *54 ft***.** Carbon Steel (SA-285 Grade C) was chosen as the material for column due its price and availability and the sieve trays were also made of Carbon Steel (SA-285 Grade C).

Using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo, the thickness and weight of the column were estimated. The weight was then used to determine the vessel cost and the purchase cost of the 20 sieve trays was also computed. The bare-module factor for the column was then determined to be 4.16 with a total bare-module cost of *$40,110,845*.

Since this is a stripping column, there is no reboiler or condenser. The only operating cost stems from the use of steam as a stripping agent. The operating cost was determined to be *$27,010,000 per year*.

When modeling the stripping column in ASPEN, the convergence of the column was highly sensitive to the flow of steam. The steam flow rate had to be gradually reduced to find the minimum flow rate that achieved our separation requirements. Carbon steel was used as the construction material due to its low costs and mild operating conditions. Design calculation initially done by hand can be found in the Appendix, and the specification sheet can be located on page 39.

3. Heat Exchangers (For the Fermenters)

The heat exchangers (Block E-12) were designed using hand calculations in Microsoft Excel. The rate of heat removal was determined based on the heat of reaction and two methods were used to estimate this quantity—the heats of formation and heats of combustion of the products and reactants. It is important to note that this method inherently assumes that the heat of metabolism of the E.coli is equal to the heat of the reaction involving the production of isoprene.

The heat of formation calculations resulted in a rate of heat removal of *4.512E+08 kJ/hr* which was equally distributed among three shell and tube heat exchangers. Initially, heating jackets and cooling coils internal to the fermenters were considered but none of these methods supplied a large enough heat transfer area for cooling. Therefore, the best option was to cool the liquid contents of the fermenters externally using an external shell and tube heat exchanger. The liquid contents were on the tube-side and the chilled water was on the shell side.

Since the fermentation temperature was 34 °C, the liquid contents were pumped out of the tank at 34 °C and were cooled to 25 °C using the heat exchanger. The cooled liquid which mainly consisted of water and dissolved gases was then pumped back into the fermenter. The CPMX property set in Aspen was used to estimate the heat capacity at constant pressure for the liquid contents of the fermenter and the molar flow rate was then computed using the specified temperature difference, required rate of heat removal, and c_p. The heat capacity of the liquid contents was *0.075 kJ/mol-K* with a molar flow rate of *493,550 lbmol/hr*.

Chilled water at 5 °C was used for the cooling and the final temperature of the water stream was determined using a ΔT_{min} of 19 °C. Therefore, the final temperature of the cooling water was 15 °C and the mass flow rate of the the cooling water was calculated using the specified temperature difference, required rate of heat removal, and c_p. The required mass flow rate of the cooling waster was *1,320,875 lbmol/hr*.

Using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo, the size of the shell and tube heat exchanger was estimated. First, the log-mean temperature difference was determined and the overall heat transfer coefficient (U) was obtained using Table 18.5 in *Product and Process Design Principles.* The heat transfer area was calculated using the required rate of heat removal, overall heat transfer coefficient, log-mean temperature difference, and correction factor (F_T). The overall heat transfer coefficient was determined to be *225 BTU/°F-ft*^{2}*-hr* and the required heat transfer area was *18806 ft*^{2}.

A tube-side velocity of 17 ft/s was chosen and the number of tubes per pass was computed assuming BWG tubing with an outer diameter of 0.75 in. and an inner diameter of

0.62 in. A tube length of 16 ft/s was selected and the number of tube passes was estimated using the heat transfer area per tube. Next, a 1-in. square pitch was assumed and the inner diameter of the shell was obtained using the tabulated data outlined in *Product and Process Design Principles.* Also, the baffle spacing was also chosen to be half of the shell diameter. The number of tubes was *991 tubes* with *7 passes*. A shell diameter of *170.32 in*. was determined and the baffle spacing was *102.19 in*.

The capital cost of each heat exchanger was estimated using the methods listed in Chapter 22 of *Product and Process Design Principles.* A fixed heat exchanger was assumed for the calculations and Carbon Steel was chosen for the shell material due to its price and availability. The shell diameter, required heat transfer area, and number of tubes were used to estimate the bare-module factor and total mare-module cost of each exchanger. Since three heat exchangers were required for our design, the total bare-module cost was determined to be *$2,065,920.14*.

The only operating costs of the heat exchangers were the utility requirements for the chilled water. The operating costs amounted to *$14,438,188.99* assuming a price of $4 per gigajoule of cooling.

Carbon steel was used as the construction material due to its low costs and mild operating conditions. Design calculation initially done by hand can be found in the Appendix, and the specification sheet can be located on page 40.

4. Heat Exchangers (For the Flash Vessel)

The heat exchanger (Block E-14) for the flash vessel's feed stream (Block E-11) was designed using a combination of our hand calculations in Microsoft Excel and Aspen simulations. The vapor product that was leaving the stripping column had to be cooled to 15 °C before it was fed to the flash vessel. The vapor phase was mainly composed of water vapor and isoprene and the cooling was required to condense isoprene out of the vapor phase.

The required rate of heat removal was first estimated using our Aspen simulation. A heater block was used to obtain the duty which was required to reduce the stripping column vapor product's temperature to 15 °C. A shell and tube heat exchanger with chilled water was used for the cooling and the chilled water was on the tube-side and the vapor phase was on the shell side. The final temperature of the chilled water stream was determined using a ΔT_{min} of 13.9 °C. Therefore, the final temperature of the chilled water was 85 °C and the mass flow rate of the the chilled water was calculated using the specified temperature difference, required rate of heat removal, and c_p. The required mass flow rate of the cooling water was 7592 *lbmol/hr*.

Using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo, the size of the shell and tube heat exchanger was estimated. First, the log-mean temperature difference was determined and the overall heat transfer coefficient (U) was obtained using Table 18.5 in *Product and Process Design Principles.* The heat transfer area was calculated using the required rate of heat removal, overall heat transfer coefficient, log-mean temperature difference, and correction factor (F_T). The overall heat transfer coefficient was determined to be *60 BTU/°F-*ft^2*-hr* and the required heat transfer area was 15,368 ft^2.

A tube-side velocity of 0.35 ft/s was chosen and the number of tubes per pass was computed assuming BWG tubing with an outer diameter of 0.75 in. and an inner diameter of 0.62 in. A tube length of 16 ft/s was selected and the number of tube passes was estimated using the heat transfer area per tube. Next, a 1-in. square pitch was assumed and the inner diameter of the shell was obtained using the tabulated data outlined in *Product and Process Design*

Principles. Also, the baffle spacing was also chosen to be half of the shell diameter. The number of tubes was *829 tubes* with *7 passes*. A shell diameter of *142.56 in*. was determined and the baffle spacing was *85.53 in*.

The capital cost of the heat exchanger was estimated using the methods listed in Chapter 22 of *Product and Process Design Principles.* A fixed heat exchanger was assumed for the calculations and Carbon Steel was chosen for the shell material due to its price and availability. The shell diameter, required heat transfer area, and number of tubes were used to estimate the bare-module factor and total mare-module cost of the exchanger. The total bare-module cost was determined to be *$337,772.49*.

The only operating costs of the heat exchangers were the utility requirements for the chilled water. The operating costs amounted to *$663,941.78* assuming a price of $4 per gigajoule of cooling.

Carbon steel was used as the construction material due to its low costs and mild operating conditions. Design calculation initially done by hand can be found in the Appendix, and the specification sheet can be located on page 41.

5. Heat Exchangers (For the Air Stream)

The heat exchanger for the air stream was designed using a similar method to that of the fermenters' heat exchangers. Hand calculations in Microsoft Excel were used to estimate the size of the heat exchanger and the detailed calculations are shown in the appendix.

A fermenter pressure of 1.7 bar was outlined in U.S. Patent Application 20130164809 and this condition was used for our process. Since ambient air is at 25 °C and 1.01 bar, the air first had to be compressed before it could be fed to the fermenter. Upon adiabatic compression, the air stream's temperature increased to 90.85 °C and it had to be cooled to 34 °C before it was fed to the fermenter. The required rate of heat removal was calculated using the heat capacity of air, the specified ΔT, and the mass flow rate of the air stream. The rate of heat removal was *7.238E+06 kJ/hr.* Also, the air stream was on the shell-side and the cooling water was on the tube-side of the heat exchanger.

Cooling water at 25 °C and 1.01 bar was used as the cold stream for the heat exchanger. The final temperature of the water stream was determined using a ΔT_{min} of 10 °C. Therefore, the final temperature of the cooling water was 80 °C and the molar flow rate of the the cooling water was calculated using the specified temperature difference, required rate of heat removal, and C_p. The required molar flow rate of the cooling water was *3260.07 lbmol/hr*.

Using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo, the size of the shell and tube heat exchanger was estimated. First, the log-mean temperature difference was determined and the overall heat transfer coefficient (U) was obtained using Table 18.5 in *Product and Process Design Principles.* The heat transfer area was calculated using the required rate of heat removal, overall heat transfer coefficient, log-mean temperature difference, and correction factor (F_T). The overall heat transfer coefficient was determined to be *60 BTU/°F-ft^2-hr* and the required heat transfer area was *6414 ft^2*.

A tube-side velocity of 0.3 ft/s was chosen and the number of tubes per pass was computed assuming BWG tubing with an outer diameter of 0.75 in. and an inner diameter of 0.62 in. A tube length of 16 ft/s was selected and the number of tube passes was estimated using the heat transfer area per tube. Next, a 1-in. square pitch was assumed and the inner diameter of the shell was obtained using the tabulated data outlined in *Product and Process Design Principles.* Also, the baffle spacing was also chosen to be half of the shell diameter. The number of tubes was *491 tubes* with *5 passes*. A shell diameter of *70.23 in*. was determined and the baffle spacing was *42.14 in*.

The capital cost of the heat exchanger was estimated using the methods listed in Chapter 22 of *Product and Process Design Principles.* A fixed heat exchanger was assumed for the calculations and Carbon Steel was chosen for the shell material due to its price and availability. The shell diameter, required heat transfer area, and number of tubes were used to estimate the bare-module factor and total mare-module cost of the exchanger. The total bare-module cost was determined to be *$115,220.99*.

The only operating costs of the air stream's heat exchanger was the utility requirements for the cooling water. The operating costs amounted to *$503,742.51* per year assuming a price of $0.02 per m^3 of cooling water.

Carbon steel was used as the construction material due to its low costs and mild operating conditions. Design calculation initially done by hand can be found in the Appendix, and the specification sheet can be located on page 42.

6. Fermenters

Since running the fermenters involves a batch process, the number of fermenters and their size were determined by making sure that a constant flow rate of off-gas from the fermenters was achieved, save for contaminations within the fermenters resulting in shutting down a tank. Thus, for a 96 hour batch cycle, it was determined that the fermenter would be in the growth phase for 8 hours to reach 15g/L E.coli. Then, the fermenter would be induced and enter the fermentation phase for 72 hours. After fermentation, the tanks would be cleaned for 10 hours with a CIP/SIP cycle. There would be 4 hours of down time for any additional checks and then 2 hours to pipe in the batch media to start the next cycle.

Based on the fact that isoprene had to be continuously produced, the water accumulation from the isoprene production reaction, feed glucose solution, and the initial batch media itself were considered. Since the necessary working volume after each 80 (8 growth + 72 fermentation) hour production cycle were known, Benz's article on fermenter sizing, "Large-Scale Microbial Production of Advanced Biofuels: How big can we go?" was used to interpolate the specifications for the fermenter vessel and agitator. This process was repeated for the seed fermenter as it was a large working volume. Finally, a rough quotation from Sartorius was obtained for the pre-seed fermenter as it is a bench-scale fermenter (5L) and was already commercially available. As such, the working volumes for the various size fermenters were 1850m^3, 88m^3, and 5L. Only the largest fermenters would be producing isoprene, and the seed and pre-seed fermenters would only be used to grow E.coli to higher concentration needed for the initial batch media for the 1850m^3 tanks.

We were provided the information that 1 gram of glucose produces 0.56 grams of biomass from Dr. Bockrath. Therefore, for our calculations of E.Coli biomass content within the fermenters and the growth of E.Coli at the beginning of each batch cycle, we used the following equation: $C_6H_{12}O_6 + 2.24\ O_2 = 4.1\ CH_{1.2}O_{0.5}N_{0.2} + 1.90\ CO_2 + 2.31\ H_2O$.

Carbon steel was used as the construction material due to its low costs and mild operating conditions. The specification sheets for the various fermenter sizes can be located on pages 44-46.

7. Flash Vessel

As was mentioned in Section 5 (Block E-10), the vapor product from the stripping column was cooled to a temperature of 15 °C in order to condense isoprene out of the vapor phase. The cooled mixed stream that was leaving the heat exchanger was fed to the flash vessel and the stream consisted of two liquid phases—a water-rich aqueous phase and an isoprene-rich organic phase—and a vapor phase.

The FLASH3 module in Aspen was used to model the flash vessel since we expected two liquid phases and one vapor phase as effluent streams. The vapor and liquid flow rates and densities of the effluents were obtained from the Aspen simulation and they were used to determine the diameter and height of the flash vessel. Using the methods outlined in *Separation Process Engineering: Includes Mass Transfer Analysis (3rd edition)* by *Phillip C. Wankat,* the diameter of the flash vessel was computed using a flooding velocity calculation. The diameter of the vessel was estimated to be *1.51 ft*. with a height of *7.55 ft*.

The capital costs of the flash vessel were computed using the methods listed in Chapter 22 of *Product and Process Design Principles.* Carbon Steel was used as the material for the vessel and the thickness and weight of the vessel were determined. These values were then used to compute the bare-module factor and total bare-module cost of the vessel. The total bare-module cost was determined to be *$48,028* with no operating costs.

Carbon steel was used as the construction material due to its low costs and mild operating conditions. Design calculation initially done by hand can be found in the Appendix, and the specification sheet can be located on page 43.

8. Storage Facilities

This process requires three main storage facilities for the isoprene product, wastewater produced at the end of each fermentation batch as it also has to sterilized before sent to wastewater treatment facilities, and sterilized media before it is pumped into fermentation tanks. We plan to have 4 days of isoprene stored as inventory, so the tank will have to able to store 600 tons or 800m^3 of isoprene if we assume that inventory will be store only for the days when the plant is operational, equal to 8000 hours.

The wastewater produced at the end of each production-level fermentation batch will have to be stored before it enters the continuous sterilization for processing before it is sent to the wastewater treatment facility. We anticipate the fermenters to run in 96 hour scheduling cycles; therefore; for a typical cycle where the 5th fermenter is not used, 9160m^3 of liquid will have be processed over 96 hours. If all fermenters failed simultaneously, the full volume of liquid must be received for wastewater treatment. However, the fermenters are staggered so that if only 1 tank is contaminated, we would only have to receive two tanks of wastewater liquid at any given time, so we suggest using a wastewater storage of 3700m^3 to accommodate any overflow.

The sterilized media will be pumped into the fermentation tanks prior to the start of each growth phase for all fermenter sizes. After accounting for the water that would be produced by the production of biomass/isoprene and the water that enters due to the glucose feed being 70% glucose, 775.7 m^3 of media will be needed for the production fermenter, 86.1 m^3 for the seed fermenter, and 4.4 L for the pre-seed fermenter. We assume that two production fermenters, one seed fermenter, and one pre-seed fermenter could possibly be need charging simultaneous, allowing for contamination and restarting batch cultures. Therefore, we suggest having a media storage of 1650 m^3 for this volume of media.

The following table shows the equipment list summary in a concise table.

Table 5. Equipment List

Block Number	Unit Type	Unit Number	Material of Construction	Size (h/l x w)	Operating T and P
E-7	Absorption Column	1	Carbon Steel	54ft x 34.8ft	34.2-34.8°C, 1.7 bar
E-9	Stripping Column	1	Carbon Steel	54ft x 39.5ft	98.8-107.8°C, 1.7 bar
E-12	Fermenter Heat Exchanger	3	Carbon Steel	16ft x 170in	1.7 bar
E-3	Air Heat Exchanger	1	Carbon Steel	16ft x 53.7in	1.7 bar
E-14	Pre-flash Heat Exchanger	1	Carbon Steel	16ft x 53.7in	1.7 bar
E-11	Flash Vessel	1	Carbon Steel	7.55ft x 1.51ft	15°C, 1.7 bar
E-5	Fermenter	5	Carbon Steel	33.2m x 9.9m	34°C, 1.7 bar
E-5	Seed Fermenter	3	Carbon Steel	12.2m x 3.6m	34°C, 1 bar
E-5	Pre-seed Fermenter	3	Carbon Steel	1.3m x 0.7m	34°C, 1 bar
N/A	Isoprene Storage Tank	1	Carbon Steel	800m^3	25°C, 1 bar
N/A	Wastewater Storage Tank	1	Carbon Steel	3700m^3	25°C, 1.7 bar
N/A	Media Storage Tank	1	Carbon Steel	1650 m^3	25°C, 1.7 bar

Specification Sheets

Absorption Column

Identification: Item Absorption Column
Item No. E-7
No. required 1

Date: 4 April 2016

By: Phillip Taylor

Function: Separate isoprene from water vapor, CO_2, Argon, and other non-condensables.

Operation: Continuous

Materials handled:	*Feed 1*	*Feed 2*	*Feed 3*	*Bottoms*	*Vapor*
Quantity (lbmol/hr):	21,597	18,298.37	116.591	18616.27	21395.76
Composition (lbmol/hr):					
Isoprene	185.5	0	33.665	215.25	3.90
Oxygen	697.5	0	1.557	1.566	697.49
Glucose	0	0	0	0	0
Carbon Dioxide	4244.81	0	55.4117	57.944	4242.27
Water	685.74	0	1.197	19.089	667.85
Nitrogen	15596.34	0	24.221	24.324	15596.23
Argon	186.34	0	0.537	0.542	186.33
Isopar	0.864	18,298.37	7.17E-05	18297.55	1.677
Temperature (°C)	34	34	15	34.85	34.18

Design Data: Number of trays: 20
Pressure: 1.7 bar
Functional Height: 54 ft
Material of construction: Carbon steel
Recommended inside diameter: 34.81 ft
Tray efficiency: 0.70
Feed 1 stage: 20
Feed 2 stage: 1
Feed 3 stage: 7

Tray spacing: 24 in.

Utilities:
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 6. Specification sheet for absorption column

Stripping Column

Identification: Item Stripping Column
Item No. E-9
No. required 1

Date: 4 April 2016
By: Phillip Taylor

Function: Separate isoprene from Isopar, water vapor, CO_2, and other non-condensables.

Operation: Continuous

Materials handled:	*Feed 1*	*Feed 2*	*Bottoms*	*Vapor*
Quantity (lbmol/hr):	18616.27	18739.29	36128.68	1226.881
Composition (lbmol/hr):				
Isoprene	215.25	0	3.83E-18	215.25
Oxygen	1.566	0	5.97E-48	1.566
Glucose	0	0	0	0
Carbon Dioxide	57.944	0	1.93E-29	57.94
Water	19.089	18739.29	17838.89	919.49
Nitrogen	24.324	0	3.91E-50	24.32
Argon	0.542	0	3.62E-50	0.542
Isopar	18297.55	0	18289.79	7.765
Temperature (°C)	34.85	115.61	107.75	98.39

Design Data: Number of trays: 20
Pressure: 1.7 bar
Functional Height: 54 ft
Material of construction: Carbon steel
Recommended inside diameter: 39.53 ft
Tray efficiency: 0.70
Feed 1 stage: 1
Feed 2 stage: 20

Tray spacing: 24 in.

Utilities:
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 7. Specification Sheet for Stripping Column

Fermenter Shell and Tube Heat Exchanger

Identification: Item Heat Exchanger
Item No. E-12
No. required 3

Date: 4 April 2016

By: Phillip Taylor

Function: Maintain a fermentation temperature of 34 °C.

Operation: Continuous

Materials handled:	*Hot In*	*Cold In*	*Hot Out*	*Cold Out*
Quantity (lbmol/hr):	493,550	1,320,875.3	493,550	1,320,875.3
Composition (lbmol/hr):				
Isoprene	1.46	0	1.46	0
Oxygen	0.54	0	0.54	0
Glucose	0	0	0	0
Carbon Dioxide	78.78	0	78.78	0
Water	493,462.97	1,320,875.3	493,462.97	1,320,875.3
Nitrogen	6.29	0	6.29	0
Argon	0.16	0	0.16	0
Isopar	0.01	0	0.01	0
Temperature (°C)	34	5	25	15

Design Data: Heat Transfer Area: 18805.64 ft^2
Type of tubing: BWG
O.D of tubing: 0.75 in.
I.D of tubing: 0.62 in.
Material of construction for shell: Carbon steel
Number of tubes per pass: 991
Length of tube: 16 ft
Number of passes 7
I.D of shell: 170.32 in.

Baffle spacing: 102.19 in.

Utilities: 1,320,875 lbmol/hr of chilled water at 5 °C and 1.01 bar.
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 8. Specification sheet for shell and tube heat exchanger for fermenters

Pre-Flash Shell and Tube Heat Exchanger

Identification: Item Heat Exchanger
Item No. E-14
No. required 1

Date: 4 April 2016
By: Phillip Taylor

Function: Maintain a flash temperature of 15 °C.

Operation: Continuous

Materials handled:	*Hot In*	*Cold In*	*Hot Out*	*Cold Out*
Quantity (lbmol/hr):	1226.881	7592.06	1226.881	7592.06
Composition (lbmol/hr):				
Isoprene	215.25	0	215.25	0
Oxygen	1.566	0	1.566	0
Glucose	0	0	0	0
Carbon Dioxide	57.94	7592.06	57.94	7592.06
Water	919.49	0	919.49	0
Nitrogen	24.32	0	24.32	0
Argon	0.542	0	0.542	0
Isopar	7.765	0	7.765	0
Temperature (°C)	98.39	5	15	85

Design Data: Heat Transfer Area: 15,368.2 ft^2
Type of tubing: BWG
O.D of tubing: 0.75 in.
I.D of tubing: 0.62 in.
Material of construction for shell: Carbon steel
Number of tubes per pass: 829
Length of tube: 16 ft
Number of passes 7
I.D of shell: 53.66 in.

Baffle spacing: 32.20 in.

Utilities: 7585.63 lbmol/hr of cooling water at 15 °C and 1.01 bar.
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 9. Specification sheet for shell and tube heat exchanger before entering flash vessel

Air Shell and Tube Heat Exchanger

Identification: Item Heat Exchanger
Item No. E-3
No. required 1

Date: 4 April 2016

By: Phillip Taylor

Function: Maintain an air temperature of 34 °C.

Operation: Continuous

Materials handled:	*Hot In*	*Cold In*	*Hot Out*	*Cold Out*
Quantity (lbmol/hr):	9686.67	3260.07	9686.67	3260.07
Composition (lbmol/hr):				
Isoprene	0	0	0	0
Oxygen	2029.36	0	2029.36	0
Glucose	0	0	0	0
Carbon Dioxide	2.62	0	2.62	0
Water	0	3260.07	0	3260.07
Nitrogen	7564.32	0	7564.32	0
Argon	90.3766	0	90.3766	0
Isopar	0	0	0	0
Temperature (°C)	90.85	30	34	80

Design Data: Heat Transfer Area: 4,363.56 ft^2
Type of tubing: BWG
O.D of tubing: 0.75 in.
I.D of tubing: 0.62 in.
Material of construction for shell: Carbon steel
Number of tubes per pass: 312
Length of tube: 16 ft
Number of passes 5
I.D of shell: 53.66 in.

Baffle spacing: 32.20 in.

Utilities: 9686.67 lbmol/hr of cooling water at 15 °C and 1.01 bar.
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 10. Specification sheet for shell and tube heat exchanger for feed gas

3 Stream Flash Vessel

Identification: Item Flash Vessel
Item No. E-11
No. required 1

Date: 4 April 2016

By: Phillip Taylor

Function: Flash the stream leaving the stripping column to separate isoprene

Operation: Continuous

Materials handled:	*Inlet*	*Vapor*	*Liquid 1*	*Liquid 2*
Quantity (lbmol/hr):	1226.881	116.591	191.3231	918.9713
Composition (lbmol/hr):				
Isoprene	215.25	33.665	181.46	0.121
Oxygen	1.566	1.557	0.00835	0.000571
Glucose	0	0	0	0
Carbon Dioxide	57.94	55.4117	1.942	0.591
Water	919.49	1.197	0.0376	918.25
Nitrogen	24.32	24.221	0.0999	0.0044
Argon	0.542	0.537	0.0047	0.0002162
Isopar	7.765	7.17E-05	7.765	4.833E-06
Temperature (°C)	15	15	15	15

Design Data: Pressure: 1.7 bar
Height: 7.55 ft
Diameter: 1.51 ft
Material of construction: Carbon steel

Utilities:
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 11. Specification sheet for 3 stream flash vessel

Fermenters

Identification: Item Fermenter
Item No. E-3
No. required 5

Date: 4 April 2016

By: Yuta Inaba

Function: Ferment E.Coli on glucose to produce isoprene

Operation: Batch

Materials handled:	*Feed Gas*	*Glucose Feed*	*Off-gas*	*Liquid Accumulation (lbmol)*
Quantity (lbmol/hr):	6901.83	873.77	7199	223511
Composition (lbmol/hr):				
Isoprene	0.67	0	61.8	0.287
Oxygen	796.2	0	232.5	0.105
Glucose	0	165.3	0	0
Carbon Dioxide	729.1	0	1414.9	15.4
Water	114.6	708.5	228.58	223494
Nitrogen	5198.8	0	5198.78	1.23
Argon	62.1	0	62.11	0.031
Isopar	0.287	0	0.288	0.003
Temperature (°C)	34	34	34	34

Design Data: Temperature: 34°C
Pressure: 1.7 bar
Working Volume: 1850 m^3
Diameter: 9.9 m
Tank Height: 33.2 m
Maximum Liquid Level: 24.7 m
Agitator Motor Size: 4770 kW
Brake Compressor Size: 8385kW
Impeller Size: 2.5m x4

Shaft Diameter: 362mm
Oxygen Transfer Rate:
200 mmol/L-hr

Utilities:
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix. Connected directly to external heat exchanger

Figure 12. Specification sheet for fermenter

Seed Fermenters

Identification: Item Fermenter
Item No. E-3
No. required 3

Date: 4 April 2016

By: Yuta Inaba

Function: Grow E.Coli to necessary concentration for the fermenter.

Operation: Batch

Materials handled:	*Batch Media*
Quantity (lbmol):	10696
Composition (lbmol):	
Isoprene	0
Oxygen	0
Glucose	28.83
Carbon Dioxide	0
Water	10667
Nitrogen	0
Argon	0
Isopar	0
Temperature (°C)	34

Design Data: Temperature: 34°C
Pressure: 1.7 bar
Working Volume: 88 m^3
Diameter: 3.6 m
Tank Height: 12.2 m
Maximum Liquid Level: 9.0 m
Agitator Motor Size: 510 kW
Brake Compressor Size: 385kW
Impeller Size: 1.3m x4

Shaft Diameter: 138 mm
Oxygen Transfer Rate:
200 mmol/L-hr

Utilities:
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix.

Figure 13. Specification sheet for seed fermenter

Pre-seed Fermenters

Identification: Item Fermenter
Item No. E-3
No. required 3

Date: 4 April 2016

By: Yuta Inaba

Function: Grow E.Coli to necessary concentration for the seed fermenter

Operation: Batch

Materials handled:	Batch Media	
Quantity (lbmol):	0.609	
Composition (lbmol):		
Isoprene	0	
Oxygen	0	
Glucose	0.001	
Carbon Dioxide	0	
Water	0.608	
Nitrogen	0	
Argon	0	
Isopar	0	
Temperature (°C)	34	

Design Data: Temperature: 34°C
Pressure: 1.7 bar
Working Volume: 5 L
Diameter: 0.7 m
Tank Height: 1.3 m
Maximum Liquid Level: 0.97 m
Agitator Motor Size: 0.5 kW
Brake Compressor Size: N/A
Impeller Size: 0.4m x6

Shaft Diameter: 138 mm
Oxygen Transfer Rate:
200 mmol/L-hr

Utilities:
Controls:
Tolerances:
Comments and drawings: See Process Flow Sheet and Appendix. Specifications obtained from Sartorius.

Figure 14. Specification sheet for pre-seed fermenter

Equipment Cost Summary

The fermenters constitute the highest equipment cost because of the numerous components required in their construction (vessel costs/agitators/etc.). The absorption and stripping column are the next highest costs, partially because of their complexity in design. The other equipment costs are much lower compared to these three parts of the plant design.

These prices were determined using the tabulated costs in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo for the various pieces of equipment.

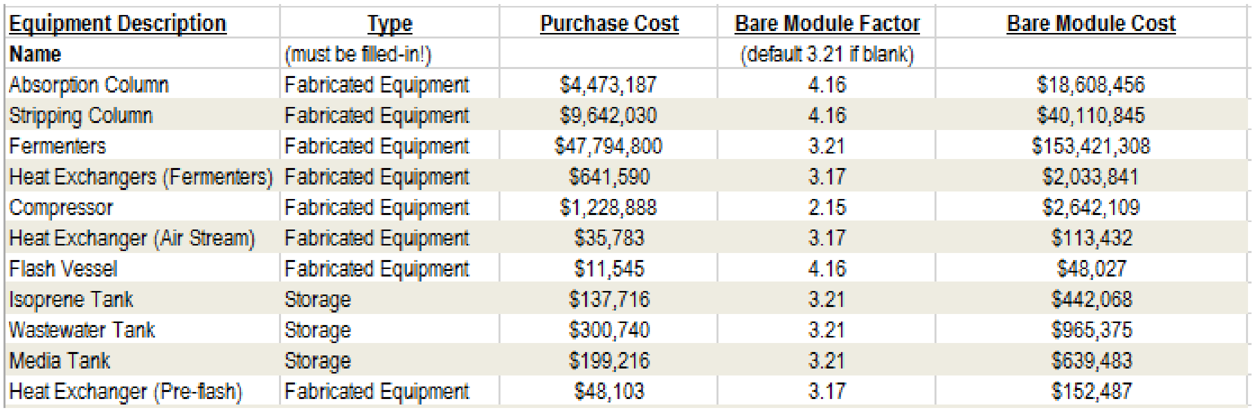
Table 6. Equipment cost summary

Equipment	Block Number	Purchase Cost
Absorption Column	E-7	$4,473,187
Stripping Column	E-9	$9,642,030
Fermenters/Agitator (all)	E-5	$47,794,800
Heat Exchangers (Fermenters)	E-12	$641,590
Compressor	E-1	$1,228,888
Heat Exchanger (Air Stream)	E-3	$35,783
Flash Vessel	E-11	$11,545
Heat Exchanger (Pre-flash)	E-14	$48,103

The purchase costs of the equipment were estimated using the methods outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo assuming a CE price index of 500. The detailed calculations are shown in the appendix.

Fixed-capital Investment Summary

The fixed-capital investment takes the purchase cost of each equipment piece and incorporates the costs of installation including direct field materials and labor, freight, overhead, and contract expenses. This adjustment in costs is lumped as a bare module factor which is a multiplicative factor for the purchase costs shown in the previous section. The total bare module cost for this process is $219,177,000.



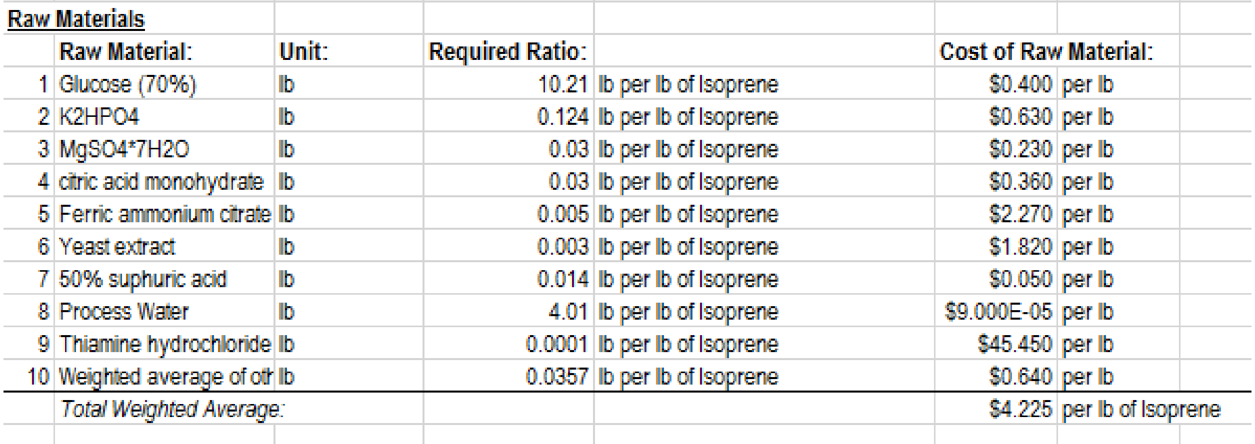
Equipment Description	Type	Purchase Cost	Bare Module Factor	Bare Module Cost
Name	(must be filled-in!)		(default 3.21 if blank)	
Absorption Column	Fabricated Equipment	$4,473,187	4.16	$18,608,456
Stripping Column	Fabricated Equipment	$9,642,030	4.16	$40,110,845
Fermenters	Fabricated Equipment	$47,794,800	3.21	$153,421,308
Heat Exchangers (Fermenters)	Fabricated Equipment	$641,590	3.17	$2,033,841
Compressor	Fabricated Equipment	$1,228,888	2.15	$2,642,109
Heat Exchanger (Air Stream)	Fabricated Equipment	$35,783	3.17	$113,432
Flash Vessel	Fabricated Equipment	$11,545	4.16	$48,027
Isoprene Tank	Storage	$137,716	3.21	$442,068
Wastewater Tank	Storage	$300,740	3.21	$965,375
Media Tank	Storage	$199,216	3.21	$639,483
Heat Exchanger (Pre-flash)	Fabricated Equipment	$48,103	3.17	$152,487

Figure 15. Bare Module Costs for equipment

Operating Cost

The operating cost of this plant includes fixed costs and variable costs. As can be seen below in Table 5, the raw materials and utilities are a significant proportion of the variable costs. Unless the cost of glucose, the major material input, is reduced, the costs incurred to produce isoprene is not favorable for this process. To produce 50,000 tons of isoprene per year, the process incurs $456 million in variable costs each year. We assumed that we would be directly receiving 70% glucose from a company like Cargill which has corn mills located in Iowa, so that we will not to have to pay transportation costs for our high consumption rate of glucose.

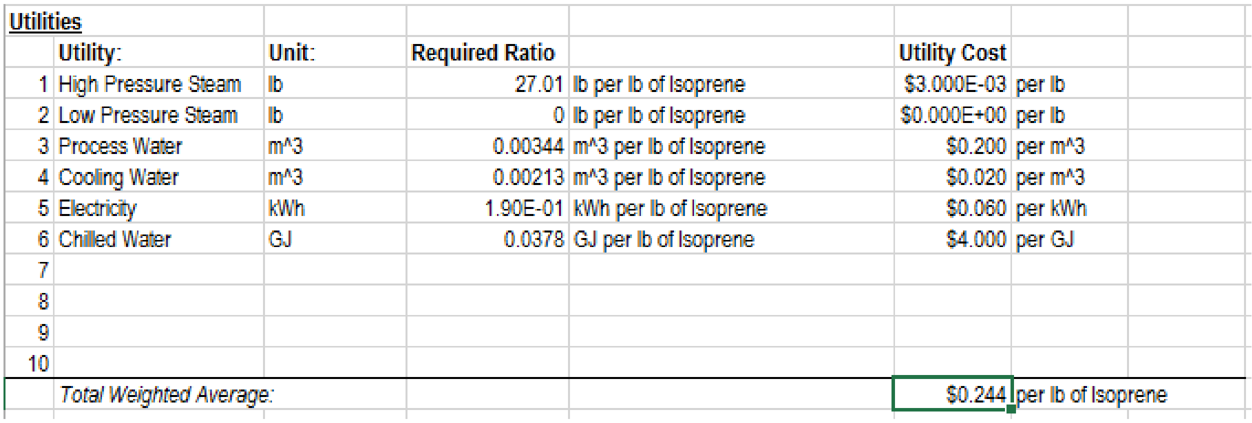
Figure 16 shows the raw materials needed for the isoprene process. Since the fermentation batch media requires many minor chemicals to be dissolved in, these prices are accounted by taking the weighted average weight and price for these compounds. Figure 17 then shows the utility costs when assuming that we would be getting our utilities provided by a nearby plant.



Raw Materials

	Raw Material:	Unit:	Required Ratio:		Cost of Raw Material:	
1	Glucose (70%)	lb	10.21	lb per lb of Isoprene	$0.400	per lb
2	K2HPO4	lb	0.124	lb per lb of Isoprene	$0.630	per lb
3	MgSO4*7H2O	lb	0.03	lb per lb of Isoprene	$0.230	per lb
4	citric acid monohydrate	lb	0.03	lb per lb of Isoprene	$0.360	per lb
5	Ferric ammonium citrate	lb	0.005	lb per lb of Isoprene	$2.270	per lb
6	Yeast extract	lb	0.003	lb per lb of Isoprene	$1.820	per lb
7	50% suphuric acid	lb	0.014	lb per lb of Isoprene	$0.050	per lb
8	Process Water	lb	4.01	lb per lb of Isoprene	$9.000E-05	per lb
9	Thiamine hydrochloride	lb	0.0001	lb per lb of Isoprene	$45.450	per lb
10	Weighted average of oth	lb	0.0357	lb per lb of Isoprene	$0.640	per lb
	Total Weighted Average:				$4.225	per lb of Isoprene

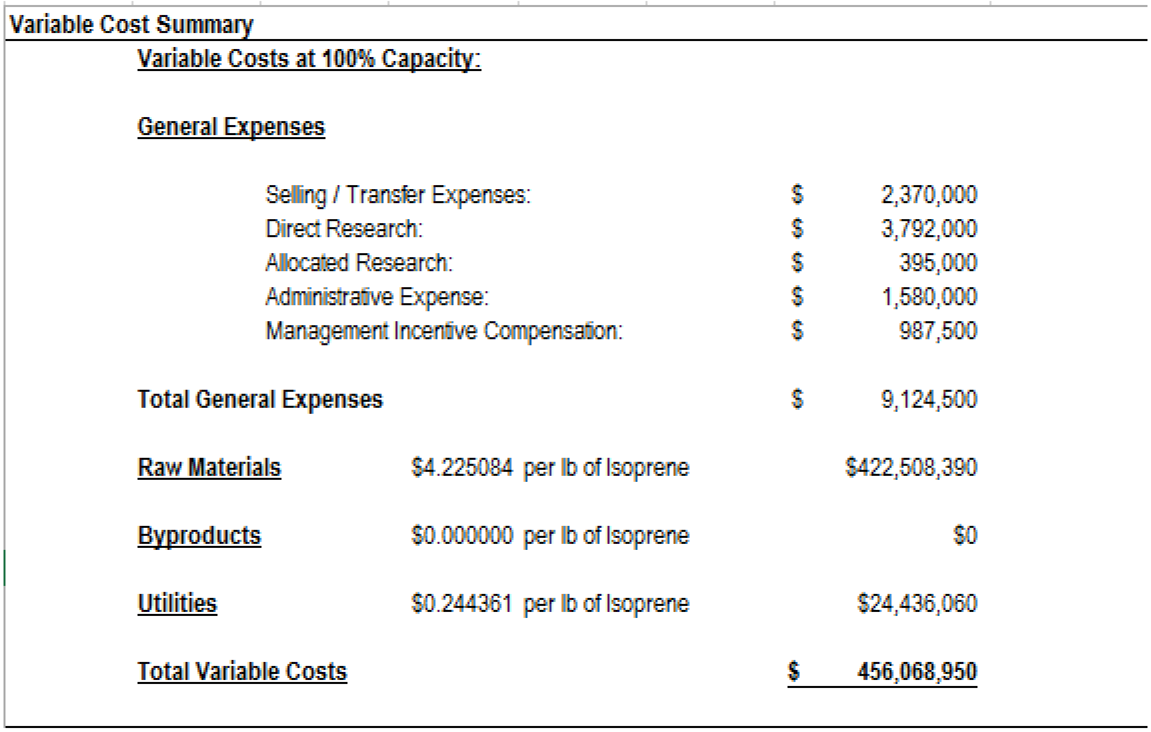
Figure 16. Raw materials variable costs



Utilities						
	Utility:	Unit:	Required Ratio		Utility Cost	
1	High Pressure Steam	lb	27.01	lb per lb of Isoprene	$3.000E-03	per lb
2	Low Pressure Steam	lb	0	lb per lb of Isoprene	$0.000E+00	per lb
3	Process Water	m^3	0.00344	m^3 per lb of Isoprene	$0.200	per m^3
4	Cooling Water	m^3	0.00213	m^3 per lb of Isoprene	$0.020	per m^3
5	Electricity	kWh	1.90E-01	kWh per lb of Isoprene	$0.060	per kWh
6	Chilled Water	GJ	0.0378	GJ per lb of Isoprene	$4.000	per GJ
7						
8						
9						
10						
	Total Weighted Average:				$0.244	per lb of Isoprene

Figure 17. Utility variable costs for isoprene

Figure 18 shows our total variable costs when general expenses are combined with the raw materials and utilities costs for production. Raw materials constitute most of our variable cost as the price of glucose is a major factor driving up the costs for this process. Our total variable cost at full capacity is $456 million.



Variable Cost Summary				
Variable Costs at 100% Capacity:				
General Expenses				
Selling / Transfer Expenses:			$	2,370,000
Direct Research:			$	3,792,000
Allocated Research:			$	395,000
Administrative Expense:			$	1,580,000
Management Incentive Compensation:			$	987,500
Total General Expenses			$	9,124,500
Raw Materials	$4.225084	per lb of Isoprene		$422,508,390
Byproducts	$0.000000	per lb of Isoprene		$0
Utilities	$0.244361	per lb of Isoprene		$24,436,060
Total Variable Costs			**$**	**456,068,950**

Figure 18. Estimate of total variable costs when producing 50,000 tons of isoprene

Table 6 lists the fixed costs of the plant. The overhead is calculated in accordance with the guidelines from *Product and Process Design Principles.* These expenses are required to operate the plant as they include operator salaries, maintenance, and general business management. The total overhead leads to an annual expense of $1.7 million.

Table 6. Fixed overhead costs per year

Fixed Costs		
Operations		
	Direct Wages and Benefits	$ 416,000
	Direct Salaries and Benefits	$ 62,400
	Operating Supplies and Services	$ 24,960
	Technical Assistance to Manufacturing	$ 300,000
	Control Laboratory	$ 325,000
	Total Operations	**$ 1,128,360**
Maintenance		
	Wages and Benefits	$ 151,913
	Salaries and Benefits	$ 37,978
	Materials and Services	$ 151,913
	Maintenance Overhead	$ 7,596
	Total Maintenance	**$ 349,399**
Operating Overhead		
	General Plant Overhead:	$ 47,449
	Mechanical Department Services:	$ 16,039
	Employee Relations Department:	$ 39,429
	Business Services:	$ 49,454
	Total Operating Overhead	**$ 152,370**
Property Taxes and Insurance		
	Property Taxes and Insurance:	$ 67,517
Other Annual Expenses		
	Rental Fees (Office and Laboratory Space):	$ -
	Licensing Fees:	$ -

	Miscellaneous:	$ -
	Total Other Annual Expenses	**$ -**
Total Fixed Costs		**$ 1,697,646**

Other Considerations

1. Safety

Isoprene is a flammable liquid and it is the only major safety hazard for our process. Isoprene must be stored and used with adequate ventilation. Its containers should be kept closed and it should be stored only where temperatures will not exceed 125 °F (52 °C). Full and empty containers of isoprene should be stored separately and a first-in, first-out inventory system should be used to prevent the storage of full containers for long periods.

There are several precautions which must be taken when handling isoprene. Inhalation and contact with eyes, skin, and clothing should be avoided. Isoprene should be kept away from heat, sparks, and open flames and only spark-proof tools and explosion-proof equipment should be used. Safety showers and eye-baths should be readily available and you should not eat, drink, or smoke in areas where isoprene is stored or used. Also, after working with this material, you should wash your face and hands thoroughly with soap and water before eating, drinking, smoking, applying cosmetics, or using the toilet. Prolonged and repeated exposure to isoprene should also be avoided.

Using the MSDS, the flammability limits for isoprene were obtained:

Lower flammability limit (in air): 1.5%

Upper flammability limit (in air): 9.7%

None of the streams in our system had an isoprene concentration that fell within the flammability limit therefore fires and explosions should not be an issue, but any changes in isoprene concentration during startup should be monitored to remain outside this range.

2. HAZOP Analysis

Since, a P&ID diagram does not exist for this process, the HAZOP analysis will instead be focused around the primary sections of the system: that is the fermentor section, the absorber and stripping section, and the storage of isoprene . The best method to prevent any kind incident and to ensure personnel safety is the use of PPE (Personal Protective Equipment).The purpose of using PPE is to protect against a majority of the hazards at the plant. Although it is subject to change depending on the materials or environment, the primary PPE that the operator should have on hand should be a hard hat, protective goggles, earplugs, hard toes shoes, gloves, and flame retardant clothing. This equipment is used to protect against any hazardous material that can contact the body, flash fires, and noise pollution that is produced due to the industrial sized equipment.

Fermenter Section:

At the fermenters, the main safety concerns that could lead to accidents or operating problems is the leakage of off gas at the outlet. This would create an asphyxiation hazard for operators at the plant. Since the offgas contains a small amount of oxygen and isoprene which can be toxic when inhaled in large amounts, proper asphyxiation safety procedures should be followed for any work done in that area. The main causes of asphyxiation hazards are failure to detect an oxygen deficient atmosphere in and around confined spaces and inadequately preparing for recognition and rescue. One primary area of concern is that there is only one operator at the plant. Should there be an incident where he finds himself in a potential low oxygen atmosphere, there will be nobody to help him. In order to prevent an incident like this from happening in the first place, a few safety measures should be implemented. For example, a continuous monitoring of oxygen deficient environments around equipment that is dealing with the off gas or isoprene. Warning systems with alarms could be implemented in order to alert the operator that an oxygen deficient environment has occurred near the equipment. Furthermore, the operator should carry a personal monitor that measures oxygen concentration in the air so that should he or she enter an area that presents a potential asphyxiation hazard, they can evacuate the area with caution and wait for further assistance.

Absorber and Stripping Column Section:

At the absorber column one safety concern is the handling of ISOPAR V. There are fire and explosion risks associated with static accumulation and discharge. In order to prevent this, the transfer system of the isopar should be effectively bound or ground in accordance with the National Fire Protection Association publications. The containers should be kept closed when not in use and should not be stored near heat, sparks, flame or strong oxidants. Although an asphyxiation hazard is also present here, it only applies towards the top of the column if any maintenance is being done.

At the stripper, the same safety concerns exist as for the absorber. However, one important additional concern is the use of steam. Since the steam is coming in at 115 degrees Celsius, it presents a burning hazard if the operator makes contact with the piping. In order to prevent this, any piping that is transporting steam needs to be insulated for heat. Not only does this prevent the loss of heat but it also help ensure safe handling of the steam piping. This also applies to the liquid stream leaving the stripper which is leaving at a temperature of 107 degrees.

For both the stripper and the absorber there are structural safety concerns due to the size of the equipment. These include vibrations, corrosion, and overheating or overpressurization. These can be solved with proper maintenance and management of the equipment so that any of these problems can be quickly identified and the proper steps can be taken to ensure they are fixed.

Isoprene Storage:

The purified isoprene at the end of the process will be stored in a storage tank. Although it is being stored as a liquid, the potential for the isoprene vaporizing towards the top of the stored liquid exists. This could cause a pressure hazard that may affect the integrity of the tank. In order to decrease this concern, a pressure relief system should be installed on the tank along with a vapor recovery system since the isoprene gas cannot be released to the environment due to EPA regulations.

3. Startup

Since the recycle loop is required for the dilution of air to an oxygen concentration of 9.97 vol%, a diluent has to be used during the startup of the process. Based on the recommendations of one of our industrial consultants, Dr. Richard Bockrath, methane gas will be burned and used as a diluent for the fermenter's air stream during startup.

It is important to note that the products of the combustion of methane include carbon dioxide and water vapor. Since a considerable amount of CO_2 will be pumped into the system during startup, this also means that the concentration of CO_2 that enters the fermenter will also be quite large. CO_2 is inhibitory to the growth of the E.coli so the initial production rate of isoprene might be below the predicted rate of 2.2 g/hr-L.

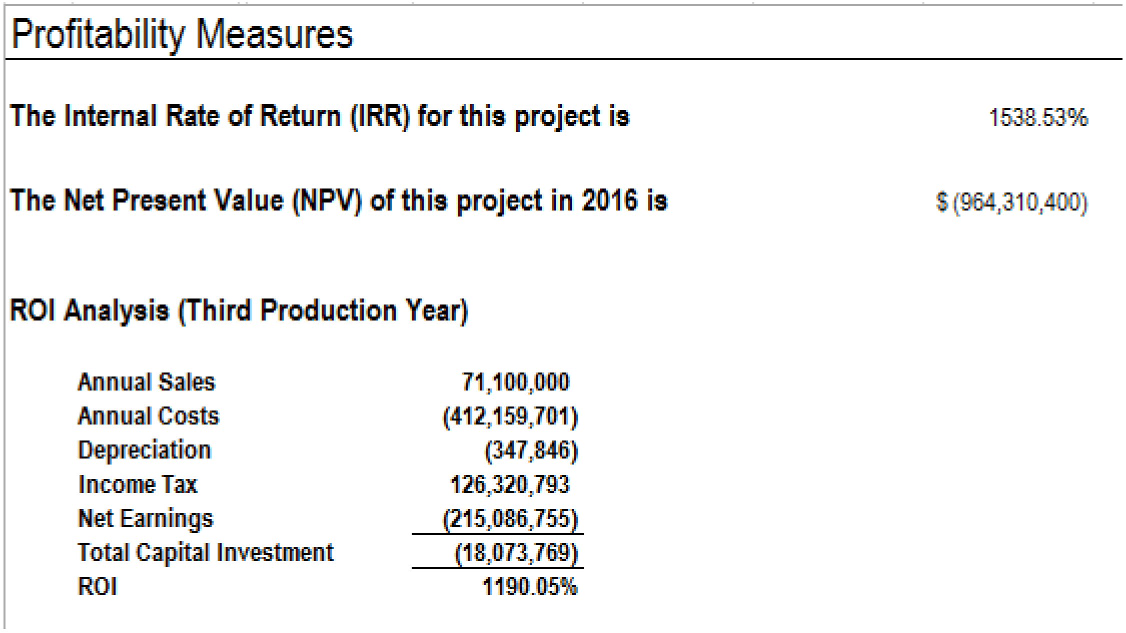
4. Environmental Concerns and Waste Removal

Wastewater treatment and disposal is one important area of consideration. As can be seen from the reaction mechanism, one of the primary byproducts from the isoprene reaction is water. Since there is an abundance of water produced there needs to be a way to treat and reuse it. The primary impurity in the water would be any dead E.coli that is left after the fermentation process is complete. This treatment process would be a two-step process. Primary treatment would include filtration of the water with coarse and fine screens and a hydrocyclone in order to remove and solids and E.Coli from the water. Secondary treatment would be a process in which we evaporate the water in four stages to recover some water to be inputted back to the process. The steam would be filtered using a scrubber. The initial three stages would be sent back as clean water and one would be sent to the waste treatment plant.

Profitability Analysis

This process is highly unprofitable due to the high operating expenses needed to produce isoprene, disregarding any capital investments needed for equipment. Due to reaction stoichiometry in the E.Coli, 10.21 lb of glucose is need per pound of isoprene. Thus, to even begin making positive revenue for this process, glucose prices will either have to drop to \$0.077/lb or isoprene prices will have to increase to \$4.084/lb. While it is difficult to foresee glucose prices falling in the future, it is possible that isoprene prices could return to prices of around \$1.50/lb. However, the current metabolic pathway does not effectively convert glucose into isoprene, resulting in a low process efficiencies.

Some profitability measures are listed below, but calculations are not required to show that there will be a high deficit from the input costs for this process. Because of the imbalance between the cash obtained from selling the isoprene to the expenses made for the raw materials, the IRR and ROI predicted for this process are unreasonably large. Without a lower input cost of glucose or a higher price of isoprene, this process will begin with a deficit, and this deficit will continue to grow as the fixed costs for purchasing equipment and other administrative costs are added. Figure 19 shows these values for completeness, but are not very useful under the assumptions we made for various prices.



Profitability Measures

The Internal Rate of Return (IRR) for this project is 1538.53%

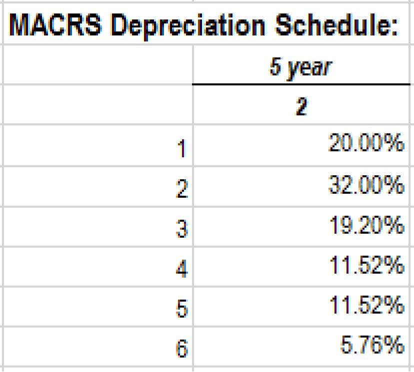
The Net Present Value (NPV) of this project in 2016 is $ (964,310,400)

ROI Analysis (Third Production Year)

Annual Sales	71,100,000
Annual Costs	(412,159,701)
Depreciation	(347,846)
Income Tax	126,320,793
Net Earnings	(215,086,755)
Total Capital Investment	(18,073,769)
ROI	1190.05%

Figure 19. Some key profitability measures for this process.

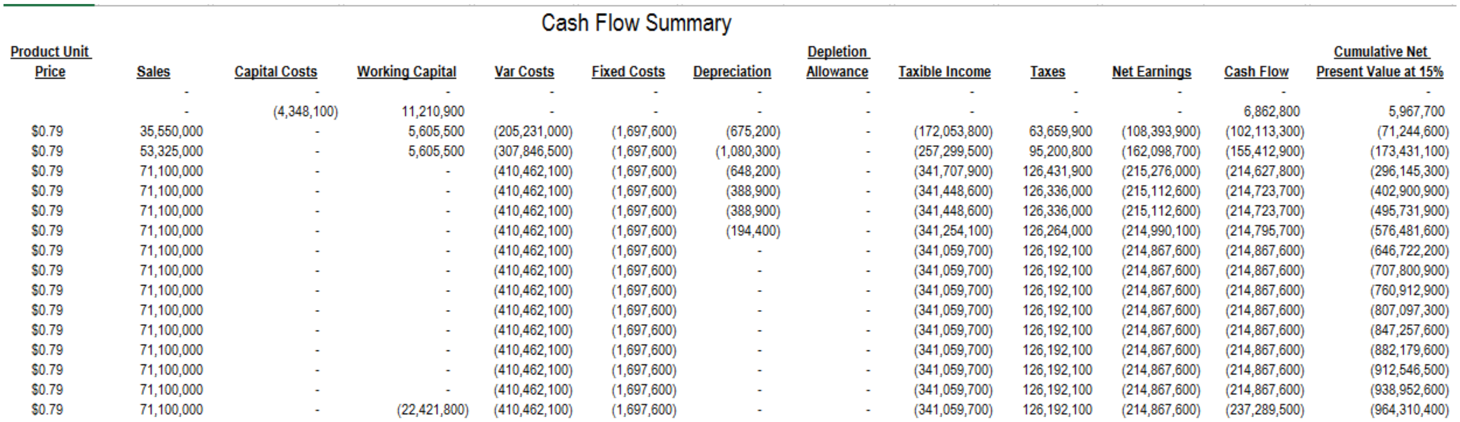
Additionally, we assumed a 5 year accelerated depreciation schedule in hopes of reducing some of our initial losses, but even with this generous assumption, our cash flows are highly negative year after year. Figure 20 shows the depreciation schedule and Figure 21 shows our yearly cash flow summary assuming that this plant will be operational for 15 years.



MACRS Depreciation Schedule:

	5 year
	2
1	20.00%
2	32.00%
3	19.20%
4	11.52%
5	11.52%
6	5.76%

Figure 20. 5 Year accelerated depreciation schedule used for the process.

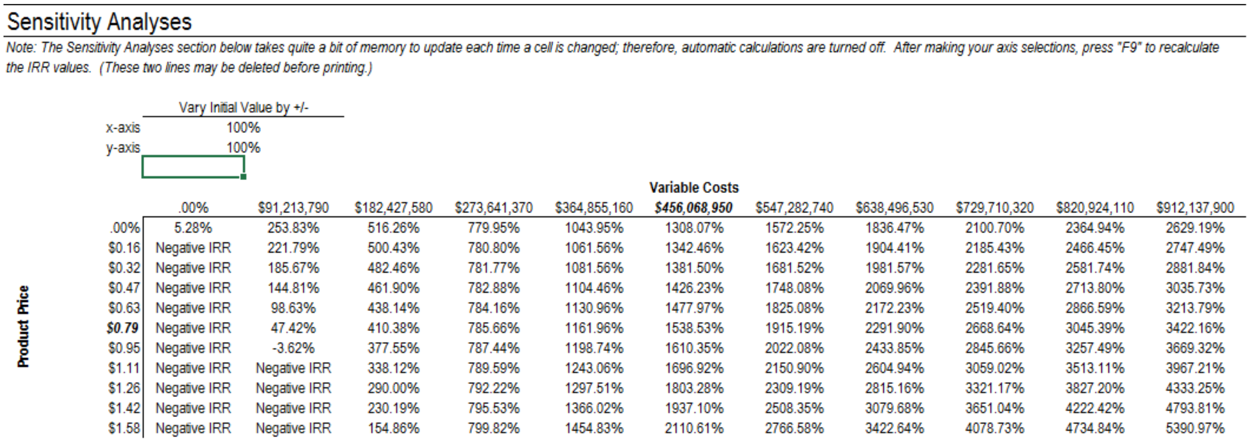


Cash Flow Summary

Product Unit Price	Sales	Capital Costs	Working Capital	Var Costs	Fixed Costs	Depreciation	Depletion Allowance	Taxible Income	Taxes	Net Earnings	Cash Flow	Cumulative Net Present Value at 15%
	-	-	-	-	-	-	-	-	-	-	-	-
	-	(4,348,100)	11,210,900	-	-	-	-	-	-	-	6,862,800	5,967,700
$0.79	35,550,000	-	5,605,500	(205,231,000)	(1,697,600)	(675,200)	-	(172,053,800)	63,659,900	(108,393,900)	(102,113,300)	(71,244,600)
$0.79	53,325,000	-	5,605,500	(307,846,500)	(1,697,600)	(1,080,300)	-	(257,299,500)	95,200,800	(162,098,700)	(155,412,900)	(173,431,100)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	(648,200)	-	(341,707,900)	126,431,900	(215,276,000)	(214,627,800)	(296,145,300)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	(388,900)	-	(341,448,600)	126,336,000	(215,112,600)	(214,723,700)	(402,900,900)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	(388,900)	-	(341,448,600)	126,336,000	(215,112,600)	(214,723,700)	(495,731,900)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	(194,400)	-	(341,254,100)	126,264,000	(214,990,100)	(214,795,700)	(576,481,600)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(646,722,200)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(707,800,900)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(760,912,900)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(807,097,300)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(847,257,600)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(882,179,600)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(912,546,500)
$0.79	71,100,000	-	-	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(214,867,600)	(938,952,600)
$0.79	71,100,000	-	(22,421,800)	(410,462,100)	(1,697,600)	-	-	(341,059,700)	126,192,100	(214,867,600)	(237,289,500)	(964,310,400)

Figure 21. Cash flow projection using a 15 year timeline

A very generous sensitivity analysis was calculating, assuming that the isoprene prices could be volatile in the upcoming years, causing the price to increase. Figure 22 shows this sensitivity analysis showing the effects of different isoprene prices and variable costs, but as stated before, the analysis is not very helpful when the process's key input component of glucose costs more than the isoprene.



Sensitivity Analyses

Note: The Sensitivity Analyses section below takes quite a bit of memory to update each time a cell is changed; therefore, automatic calculations are turned off. After making your axis selections, press "F9" to recalculate the IRR values. (These two lines may be deleted before printing.)

	Vary Initial Value by +/-
x-axis	100%
y-axis	100%

						Variable Costs					
Product Price	.00%	$91,213,790	$182,427,580	$273,641,370	$364,855,160	***$456,068,950***	$547,282,740	$638,496,530	$729,710,320	$820,924,110	$912,137,900
.00%	5.28%	253.83%	516.26%	779.95%	1043.95%	1308.07%	1572.25%	1836.47%	2100.70%	2364.94%	2629.19%
$0.16	Negative IRR	221.79%	500.43%	780.80%	1061.56%	1342.46%	1623.42%	1904.41%	2185.43%	2466.45%	2747.49%
$0.32	Negative IRR	185.67%	482.46%	781.77%	1081.56%	1381.50%	1681.52%	1981.57%	2281.65%	2581.74%	2881.84%
$0.47	Negative IRR	144.81%	461.90%	782.88%	1104.46%	1426.23%	1748.08%	2069.96%	2391.88%	2713.80%	3035.73%
$0.63	Negative IRR	98.63%	438.14%	784.16%	1130.96%	1477.97%	1825.08%	2172.23%	2519.40%	2866.59%	3213.79%
$0.79	Negative IRR	47.42%	410.38%	785.66%	1161.96%	1538.53%	1915.19%	2291.90%	2668.64%	3045.39%	3422.16%
$0.95	Negative IRR	-3.62%	377.55%	787.44%	1198.74%	1610.35%	2022.08%	2433.85%	2845.66%	3257.49%	3669.32%
$1.11	Negative IRR	Negative IRR	338.12%	789.59%	1243.06%	1696.92%	2150.90%	2604.94%	3059.02%	3513.11%	3967.21%
$1.26	Negative IRR	Negative IRR	290.00%	792.22%	1297.51%	1803.28%	2309.19%	2815.16%	3321.17%	3827.20%	4333.25%
$1.42	Negative IRR	Negative IRR	230.19%	795.53%	1366.02%	1937.10%	2508.35%	3079.68%	3651.04%	4222.42%	4793.81%
$1.58	Negative IRR	Negative IRR	154.86%	799.82%	1454.83%	2110.61%	2766.58%	3422.64%	4078.73%	4734.84%	5390.97%

Figure 22. Sensitivity analysis on price of isoprene and variable costs

Conclusions and Recommendation

The production of isoprene via the fermentation of glucose is a novel yet unprofitable venture. Based on the results of our analysis, we have concluded that our design simply does not have a competitive advantage. The price of isoprene is too low when compared to the costs of raw materials and the chemical pathway for the production of isoprene is also highly exothermic. The large rate of heat removal for the fermenters resulted in astronomically large utility requirements for chilled water. Another issue is that the fermentation has to be operated at a pressure of 1.7 bar. The electricity costs due to the use of a compressor were considerable and large amounts of Isopar and steam were required for the absorption and stripping columns.

As for any plant design, there is certainly room for improvement regarding our current design. One method which would decrease the raw material costs is that stream 19—i.e. the liquid product leaving the stripping column—could be recycled back to the absorption column. The liquid product leaving the stripping column is rich in Isopar and the reuse of the solvent would significantly decrease the plant's operating costs. Another issue is that the isoprene product is obtained as a liquid (stream 25) with a purity of approximately 95%. The purity of the isoprene product can be increased to 99% by adding a second flash vessel which would separate the isoprene from the remaining Isopar that is present in stream 25.

A third recommendation is that the isoprene that's lost at the end of every fermentation batch can be recycled. Isoprene is immiscible with water so the liquid contents of the fermenter is essentially a two-phase system—an isoprene-rich phase and an aqueous phase. A decanter can be used to separate the two immiscible layers and the isoprene layer could be obtained with a fairly high purity. Based on our estimates, 0.85 lbmol of isoprene are being lost per fermentation batch which amounts to a total of 95.5 lbmol of isoprene which can be recovered per year.

Acknowledgments

Thanks to Dr. Sue Ann Bidstrup-Allen, Dr. Richard Bockrath, and all of our other industrial advisors for their assistance and support during the design of this process. Special thanks are also sent to Professor Leonard Fabiano for his guidance regarding the design of our Aspen flow sheet and his efforts to contact the AspenTech support team.

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Appendix

1. **Hand Calculations—Material Balances (Option B)**

The material balances for the system were first solved by hand using Microsoft Excel. The resulting flow rates for the air stream, fermenter feed, and split fraction for the purge were used as inputs for the Aspen simulation. There were five major assumptions that were made in solving these material balances:

(1) The vapor product from the absorption column contained a negligible concentration of water. It was assumed that all of the water would condense in the absorption column.

(2) There was a perfect separation between isoprene and the other gas phase components at the absorption column. This assumption is unrealistic but it allowed for an estimate of the required air flow rate and split fraction for the process.

(3) The vapor feed stream entering the fermenter contained oxygen in 20% excess of the stoichiometric amount that was required to produce 50,000 ton of isoprene per year.

(4) The vapor feed stream to the fermenter had an oxygen concentration of 9.97 vol%.

(5) Since the target oxygen concentration was given in terms of a volume percentage, it was assumed that the vapor feed to the fermenter behaved ideally. This allowed us to use the volume percentage of oxygen as a molar percentage in the material balances.

The results of our excel spreadsheet are shown on the next page:

Option B (Recycle)			**Assumptions: 20% excess O2 and 9.97 vol% O2 in Fermenter Feed**
Stoichiometric amount of glucose required (not including cell growth)	3.749E+03	mol/min	
Stoichiometric amount of water produced	1.695E+04	mol/min	
Stoichiometric amount of oxygen needed	1.279E+04	mol/min	
Stoichiometric amount of CO2 produced	1.556E+04	mol/min	
Molar flow rate of Air	7.323E+04	mol/min	
Molar flow rate of Purge	7.601E+04	mol/min	(This value assumes that the mass frac. of H2O in the purge is negligible)
Molar Flow Rate of Fermenter Feed Stream	1.539E+05	mol/min	
Molar Flow Rate of Recycle	8.065E+04	mol/min	
Split Fraction	0.485	(being purged)	
Mole Fractions of Purge and Recycle:			
Mole Fraction of N2	0.752		
Mole Fraction of O2	0.034		
Mole Fraction of Ar	0.009		
Mole Fraction of CO2	0.205		
Sum of mole fractions	1.000	(great!)	
Mole Fractions of Feed Stream to Fermenters:			
Mole Fraction of N2	0.766		

Mole Fraction of O2	**0.1173**		
Mole Fraction of Ar	0.009		
Mole Fraction of CO2	0.108		
Sum of mole fractions	1.000	(great!)	
Feed Stream to Absorber:			
Molar Flow Rate	1.603E+05	mol/min	(This assumes the exit stream leaving the fermenter is saturated with H2O)
Composition of Feed to Absorber:			
Mole Fraction of N2	0.735		
Mole Fraction of O2	0.016		
Mole Fraction of isoprene	0.009		
Mole Fraction of Ar	0.009		
Mole Fraction of CO2	0.200		
Mole Fraction of H2O	0.031		
Sum of mole fractions	1.000	(great!)	
Liquid Water leaving through the fermenter	1.198E+04	mol/min	
Flow rate of isoprene-lean gas stream	1.539E+05	mol/min	(This assumes a perfect separation between isoprene and the other gas-phase components)
(i.e. the gas stream leaving the top of the tower)			
Composition of isoprene-lean gas stream:			
Mole Fraction of N2	0.766		
Mole Fraction of O2	0.017		
Mole Fraction of Ar	0.009		

Mole Fraction of CO2	0.209		
Sum of mole fractions	1.000		

2. Hand Calculations—Material Balances (Option A)

The material balances for option A were solved assuming a production target of 50,000 ton of isoprene per year. There were four major assumptions which were made in solving these material balances.

(1) There was a perfect separation between isoprene and the other gas phase components at the absorption column. This assumption is unrealistic but it allowed for an estimate of the required air flow rate for the process.

(2) The vapor feed stream entering the fermenter contained oxygen in 20% excess of the stoichiometric amount that was required to produce 50,000 ton of isoprene per year.

(3) The vapor feed stream to the fermenter had an oxygen concentration of 9.97 vol%.

(4) Since the target oxygen concentration was given in terms of a volume percentage, it was assumed that the vapor feed to the fermenter behaved ideally. This allowed us to use the volume percentage of oxygen as a molar percentage in the material balances.

The results of our spreadsheet are shown below:

Option A (Using membranes)				
Air	%	**Assumption:**	**8000 working hours / yr**	
Nitrogen	78.09	vol %	75.47	wt %
Oxygen	20.95	vol %	23.2	wt %

Argon	0.933	vol %	1.28	wt %
Carbon Dioxide	0.027	vol %	0.05	wt %
Necessary O2	1.38E+11	L/yr	2.86E+05	L/min
Necessary Air	6.56E+11	L/yr	1.37E+06	L/min
Necessary N2 diluent	7.23E+11	L/yr	1.51E+06	L/min
Total Gas Inflow	1.38E+12	L/yr	2.87E+06	L/min
N2 moles	3.23E+10	moles		
N2 mass	9.04E+08	kg		
Liquid N2 vol	1.12E+06	m^3		
	2.95E+08	gal/yr		
Liquid N2 vol	8.86E+05	gal/day		
CO2 Volume	1.67E+11	L/yr		
H2O moles	8.14E+09	moles/yr		
H2O vol, liquid	4.52E+02	m^3/yr		

3. Hand Calculations—Absorption Column

The number of actual stages for the column was estimated using the Kremser equation. The calculations of the absorption factor, minimum flow rate of solvent required, and number of stages are shown on the next page.

Kremser Calculations (Absorption)		
Entering vapor flow rate to absorption column (V)	9.618E+03	kmol/hr
I'll use Raoult's Law to calculate the K-value of isoprene:		
K-value of isoprene	0.591	
(1 - phi)	0.9999	
Lmin (minimum amount of absorbent rate)	**5.682E+03**	kmol/hr
I'll choose an operating absorbent flow rate of 1.5*Lmin		
L	**8.523E+03**	kmol/hr
Absorption factor (A)	1.50	(Eq. 19.2)
Number of stages	20	stages

The diameter and height of the column were estimated using a flooding velocity calculation outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo. The flow rates and densities for liquid and vapor products of the column were obtained from our Aspen simulation. The estimates for the capacitance parameter, surface tension factor, foaming factor, and hole-area factor were computed using the aforementioned methods.

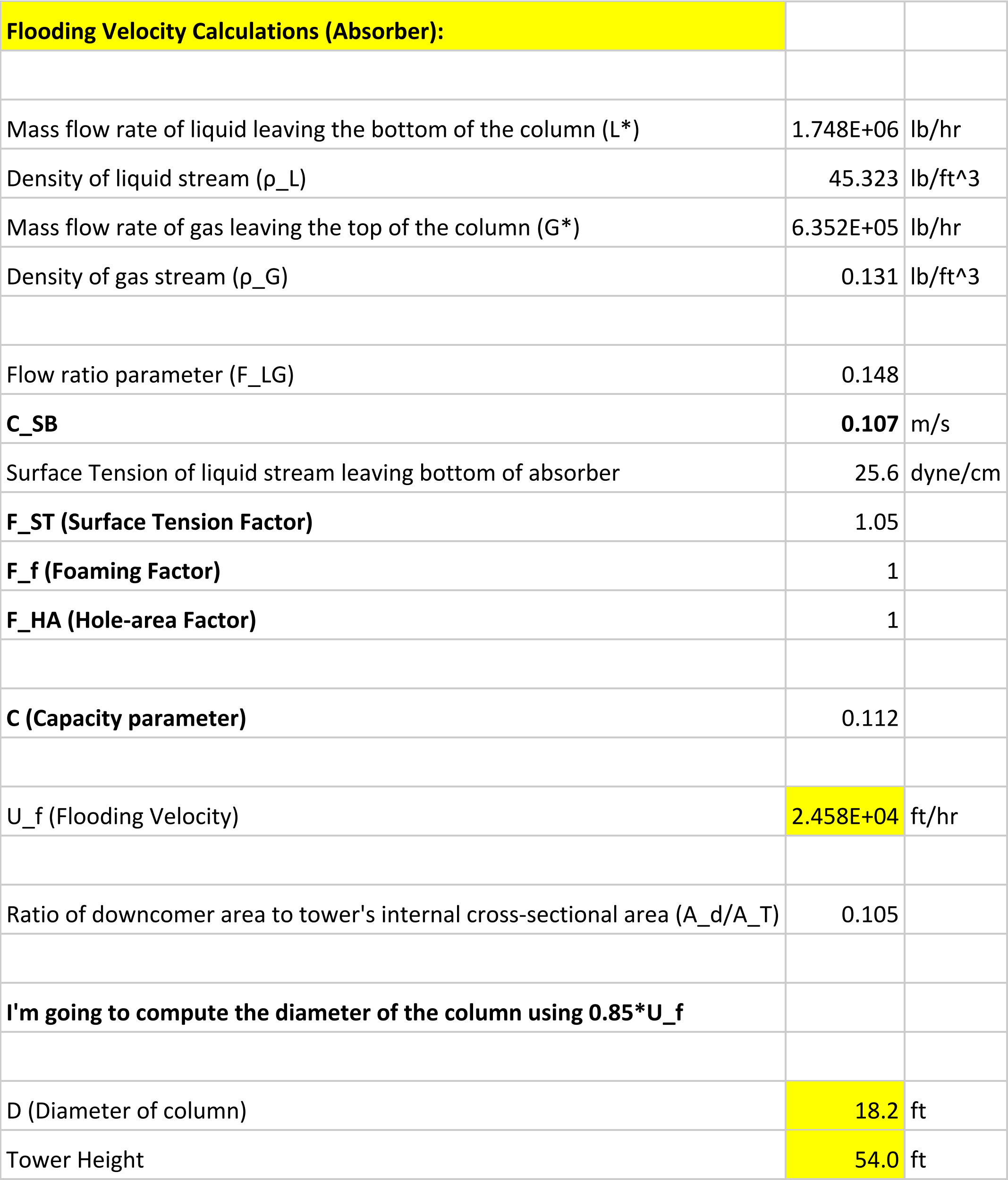
The following assumptions were made for the flooding velocity calculations:

(1) A tray column will be used with 24 in. spacing between trays.

(2) The trays are non-foaming.

(3) Sieve trays will be used.

The results of our Excel spreadsheet are shown on the next page.



Flooding Velocity Calculations (Absorber):		
Mass flow rate of liquid leaving the bottom of the column (L*)	1.748E+06	lb/hr
Density of liquid stream (ρ_L)	45.323	lb/ft^3
Mass flow rate of gas leaving the top of the column (G*)	6.352E+05	lb/hr
Density of gas stream (ρ_G)	0.131	lb/ft^3
Flow ratio parameter (F_LG)	0.148	
C_SB	**0.107**	m/s
Surface Tension of liquid stream leaving bottom of absorber	25.6	dyne/cm
F_ST (Surface Tension Factor)	1.05	
F_f (Foaming Factor)	1	
F_HA (Hole-area Factor)	1	
C (Capacity parameter)	0.112	
U_f (Flooding Velocity)	2.458E+04	ft/hr
Ratio of downcomer area to tower's internal cross-sectional area (A_d/A_T)	0.105	
I'm going to compute the diameter of the column using 0.85*U_f		
D (Diameter of column)	18.2	ft
Tower Height	54.0	ft

Note: The diameter and height that were obtained using our hand calculations were **not** used in our profitability analysis. Aspen's estimates were used instead.

4. Hand calculations—Stripping Column

The number of actual stages for the column was estimated using the Kremser equation. The calculations of the stripping factor, minimum flow rate of steam required, and number of stages are shown below:

Kremser Calculations (Stripping)		
Entering liquid flow rate to stripping column (L)	**8.606E+03**	kmol/hr
I'll use Raoult's Law to calculate the K-value of isoprene:		
K-value of isoprene	11.259	
(1 - phi)	0.9999	
Vmin (minimum flow rate of stripping agent)	7.643E+02	kmol/hr
I'll choose an operating stripping agent flow rate of 1.5*Vmin		
V	1.146E+03	kmol/hr
Stripping factor (S)	1.50	
Number of stages	**20**	

The diameter and height of the column were estimated using a flooding velocity calculation outlined in *Product and Process Design Principles* by Seider, Seader, Lewin, and Widagdo. The flow rates and densities for liquid and vapor products of the column were obtained from our Aspen simulation. The estimates for the capacitance parameter, surface tension factor, foaming factor, and hole-area factor were computed using the aforementioned methods.

The following assumptions were made for the flooding velocity calculations:

(1) A tray column will be used with 24 in. spacing between trays.

(2) The trays are non-foaming.

(3) Sieve trays will be used.

The results of our Excel spreadsheet are shown below.

Flooding Velocity Calculations (Stripping)		
Mass flow rate of liquid leaving the bottom of the column (L*)	3.043E+06	lb/hr
Density of liquid stream (ρ_L)	43.412	lb/ft^3
Mass flow rate of gas leaving the top of the column (G*)	6.968E+05	lb/hr
Density of gas stream (ρ_G)	0.079	lb/ft^3
Flow ratio parameter (F_LG)	0.187	
C_SB	**0.099**	m/s
Surface Tension of liquid stream leaving bottom of absorber	17.8	dyne/cm
F_ST (Surface Tension Factor)	0.98	
F_f (Foaming Factor)	1	
F_HA (Hole-area Factor)	1	
C (Capacity parameter)	0.097	
U_f (Flooding Velocity)	2.673E+04	ft/hr
Ratio of downcomer area to tower's internal cross-sectional area (A_d/A_T)	0.110	
I'm going to compute the diameter of the column using 0.85*U_f		
D (Diameter of column)	23.5	ft
Tower Height	54.0	ft

Note: The diameter and height that were obtained using our hand calculations were **not** used in our profitability analysis. Aspen's estimates were used instead.

5. Hand Calculations—Shell and Tube Heat Exchanger (Fermenters)

The calculations of the sizes and flow rates for the fermenter's shell and tube heat exchangers were described in the Equipment List and Unit Descriptions section. The results of our excel spreadsheet are shown below.

Heat Exchangers for Fermenters		
Total Q	-4.512E+08	kJ/hr
Q per fermenter	-1.504E+08	kJ/hr
Using Aspen, I obtained the heat capacity for the liquid that's leaving the fermenter		
Cp	0.0745814736	kJ/mol-K
Upper limit on the fermenter's temperature	34	°C
Target Temperature	25	°C
Molar flow rate of hot stream to the heat exchanger	**2.241E+08**	mol/hr
We're using cooling water at 5°C and 1 atm		
Initial temperature of cooling water	5	°C
Final temperature of cooling water	15	°C
Mass flow rate of cooling water	**3.598E+06**	kg/hr
Note: We'll need five identical heat exchangers (only three will be operated at any given time)		
Total cooling water requirement for fermenters	**1.079E+07**	kg/hr
Sizing Calculations for Heat Exchangers (for fermenters):		
Log-mean temperature difference	35.09	°F

Next, I estimated the overall heat transfer coefficient using Table 18.5 in the Product and Process Design text)		
Note: This assumes that the cooling water is on the *shell* side and the liquid that's leaving the fermenter is on the *tube* side		
U	225	BTU/°F-ft^2-hr
Next, I need to estimate the correction factor F_T		
R	0.900	
S	0.345	
F_T (Correction Factor)	0.959	
Ai (Heat Transfer Area)	**18805.64**	ft^2
I'm going to select a stream velocity of 17 ft/s for the tube side:		
u	17	ft/s
Total cross-sectional area per pass	2.077	ft^2
Assuming that we have tubes with the following sizes:		
O.D	0.75	in
I.D	0.62	in
Number of tubes per pass	**991**	tubes
I'm going to select a tube length of 16 ft		
L	16	ft
Heat transfer area per tube	2.597	ft^2
Number of tube passes	**7**	passes
Assuming the tubes are on a 1-in square pitch		
Total number of tubes	7241	tubes
Inner Diameter of Shell (D_s)	**170.32**	in
Baffle spacing:		
b_min	34.06498257	in

b_max	170.32	in
I'm going to select a baffle spacing that's directly in the midle of this range		
b	**102.19**	in

6. Hand Calculations—Shell and Tube Heat Exchanger (Air Stream)

The calculations of the sizes and flow rates for the air stream's shell and tube heat exchanger were described in the Equipment List and Unit Descriptions section. The results of our excel spreadsheet are shown below.

Sizing Calculations (for the air stream's HX)		
Mass flow rate of air stream	1.273E+05	kg/hr
Initial temp of air	90.84755	°C
Final temp of air	34	°C
Heat capacity of air	1.0005	kJ/kg-K
Q	7.238E+06	kJ/hr
Initial temp of cooling water	25	°C
Final temp of cooling water	80	°C
Mass flow rate of cooling water	**3.148E+04**	kg/hr
Log-mean temperature difference	17.811	°F
Next, I estimated the overall heat transfer coefficient using Table 18.5 in the Product and Process Design text)		
Note: This assumes that the cooling water is on the *tube* side and air is on the *shell* side		
U	60	BTU/°F-ft^2-hr

Next, I need to estimate the correction factor F_T		
R	1.034	
S	0.835	
F_T (Correction Factor)	1.000	(I'll fix this later)
Ai (Heat Transfer Area)	**6,414.10**	ft^2
I'm going to select a stream velocity of 0.4 ft/s for the tube side:		
u	0.3	ft/s
Total cross-sectional area per pass	1.030	ft^2
Assuming that we have tubes with the following sizes:		
O.D	0.75	in
I.D	0.62	in
Number of tubes per pass	**491**	tubes
I'm going to select a tube length of 16 ft		
L	16	ft
Heat transfer area per tube	2.597	ft^2
Number of tube passes	**5**	passes
Assuming the tubes are on a 1-in square pitch		
Total number of tubes	2470	tubes
Inner Diameter of Shell (D_s)	**70.23**	in
Baffle spacing:		
b_min	14.04517081	in
b_max	70.23	in
I'm going to select a baffle spacing that's directly in the midle of this range		
b	**42.14**	in

7. Hand Calculations—Shell and Tube Heat Exchanger (Flash Vessel)

The calculations of the sizes and flow rates for the heat exchanger for the flash vessel's feed were described in the Equipment List and Unit Descriptions section. The results of our excel spreadsheet are shown below.

Sizing Calculations (HX for the Flash Vessel's Feed)		
Required Heat Duty	20748180.72	kJ/hr
Inlet temp. of vapor stream	98.9	°C
Outet temp. of vapor stream	15	°C
Initial temp. of chilled water	5	°C
Final temp. of chilled water	85	°C
Note: We're using chilled water at 5 degrees C and 1 atm		
Mass flow rate of chilled water	61986.68	kg/hr
Log-mean temperature difference	21.309	°F
Next, I estimated the overall heat transfer coefficient using Table 18.5 in the Product and Process Design text)		
Note: This assumes that the cooling water is on the *tube* side and the vapor is on the *shell* side		
U	60	BTU/°F-ft^2-hr
Next, I need to estimate the correction factor F_T		
R	1.05	
S	0.852	
F_T (Correction Factor)	1.000	

Ai (Heat Transfer Area)	**15368.13893**	ft^2
I'm going to select a stream velocity of 17 ft/s for the tube side:		
u	0.35	ft/s
Total cross-sectional area per pass	1.738	ft^2
Assuming that we have tubes with the following sizes:		
O.D	0.75	In.
I.D	0.62	In.
Number of tubes per pass	**829**	
I'm going to select a tube length of 16 ft		
L	16	ft
Heat transfer area per tube	2.597	ft^2
Number of tube passes	**7**	
Assuming the tubes are on a 1-in square pitch		
Total number of tubes	5918	
Inner Diameter of Shell (D_s)	**142.56**	**in**
Baffle spacing:		
b_min	28.5113439	
b_max	142.56	
I'm going to select a baffle spacing that's directly in the midle of this range		
b	**85.53**	**in**

8. Hand Calculations—Flash Vessel

As was mentioned in the Equipment Lists and Unit Descriptions section, the diameter and height of the flash vessel were computed using the methods outlined in *Separation Process Engineering: Includes Mass Transfer Analysis (3rd edition)* by *Phillip C. Wankat.* A flooding velocity calculation was used and 85% of the flooding velocity was chosen. The detailed calculations are shown below:

Flash Vessel Sizing		
Liquid flow rate	30458.57	lb/hr
Vapor flow rate	5503.329	lb/hr
Density of liquid phase	53.66	lb/ft^3
Density of vapor phase	0.21	lb/ft^3
F_lv	0.348	
K_drum	0.298	ft/s
U_perm	4.72	ft/s
We're going to use 85% of the flooding velocity for our calculations		
U	4.016024592	ft/s
Cross-sectional area (A_c)	1.79056846	ft^2
Diameter of flash vessel	**1.51**	ft
Assuming a height-to-diameter ratio of 5		
Height of flash vessel	**7.55**	ft

9. Aspen Flow Sheet

The Aspen flow sheet is essentially the same as the process flow diagram. The only notable difference is that the fermenters were modeled using the RSTOIC and flash vessel modules in Aspen. Since it isn't possible to specify two separate phases as effluent streams for RSTOIC, a flash vessel had to be used to separate the liquid and vapor phases for the fermenter.

Even though the fermenter was modeled as a continuous process, it is in fact a batch process. Our scheduling of the fermenters allowed for the continuous production of isoprene in the vapor phase but the liquid phase; however, was removed at the end of every 72 hour batch. Even though a continuous process was simulated, the results of the simulations were used to estimate the compositions of the vapor and liquid phases of the fermenter, which were valid even though the removal of the liquid contents of the fermenters was inherently a batch process. Therefore, it allowed us to estimate the amount of isoprene that was lost after every fermentation batch since the flow rate of the liquid phase was easily converted to a batch value. The amount of liquid that accumulated in the fermenter was simply 72 hours times the liquid flow rate that was obtained from Aspen.

The other unit operations are the same as the ones that were listed in the process flow sheet, and no further explanations are necessary.