Team 6: Sustainable Hyaluronic Acid Production Enhancement (SHAPE)

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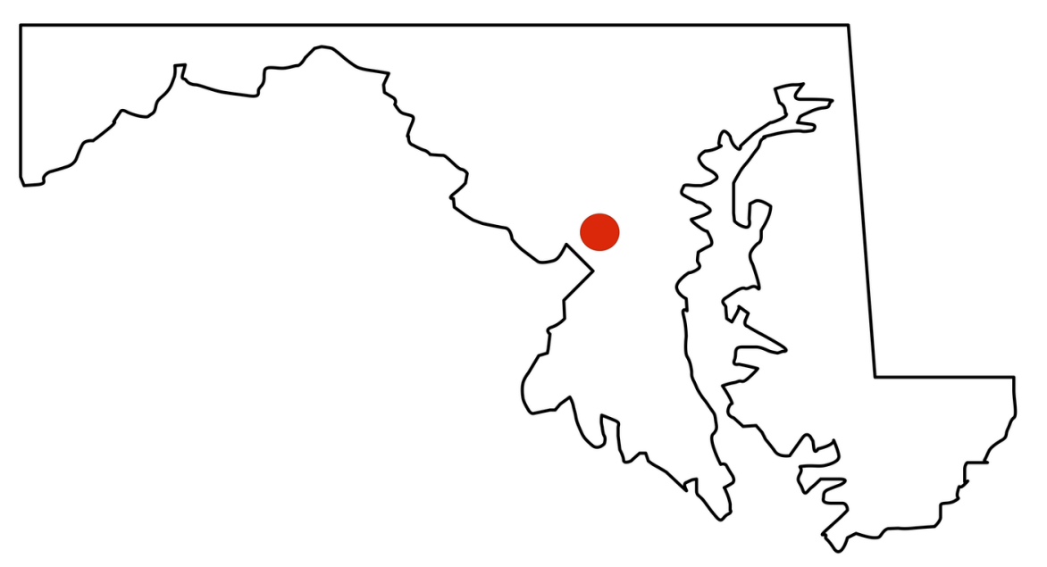


Project 1: DIB Tower Electrification

Electrification of distillation columns is the process of replacing modes of system heating from fossil fuel sources to those electrically powered, as a means to be more environmentally sustainable and energetically efficient. In this project, a heat pump system is considered to extract heat released by the condenser and use this to power the reboiler.

Base-Case Design

- 57-stage distillation tower to separate a mixture of n-butane and iso-butane, with feed entering above stage 50
    - Distillate is rich in isobutane
    - Bottoms is rich in normal butane
- Utilizes total condenser and reboiler to return material back into the column for further separation
- Requires cooling water and low pressure steam as externally supplied utilities

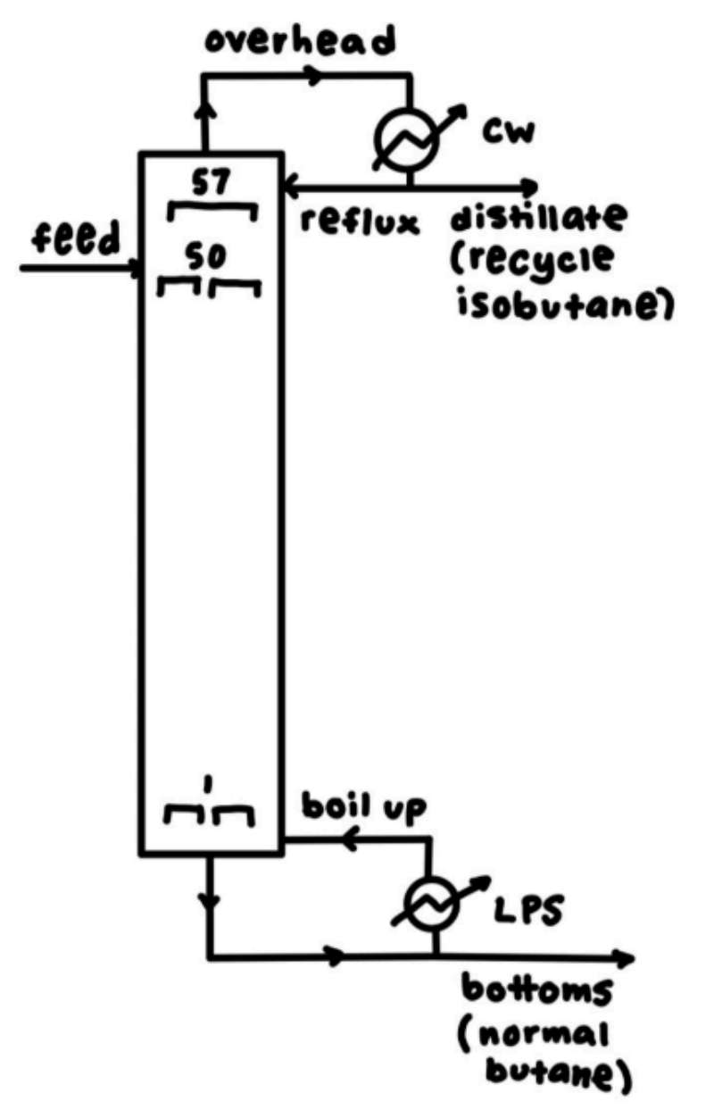


Figure 1: Base case deisobutanizer column

Heat Pump Design

- Operating temperature window: 39.75 - 58.55 C
- 2 working fluids were considered: ammonia (R717) and 1,1,1,2-tetrafluoroethane (R134a)
    - R717: higher circulation rate, larger pump equipment, chemically hazardous, low emissions
    - R134a: lower circulation rate, smaller pump equipment, chemically safe, high emissions
    - → **R717 was deemed the more sustainable working fluid choice**
- Design changes: addition of expansion valve, compressor, external piping,
- Additional controls systems to implement a finite-state machine:
    - Thermocouples (every 5-10 trays, reboiler, condenser)
    - Temperature transmitters (TT), temperature indicator controller
    - Pressure transmitter (PT) (column overhead and bottoms)
    - Pressure indicater controller (PIC), pressure safety valves/pressure relief system
    - Flow transmitters (FT), Flow indicator controllers (FIC) (inlet or outlet streams)
    - Distributed control system (DCS), DCS-based alarm system, emergency shutdown valves

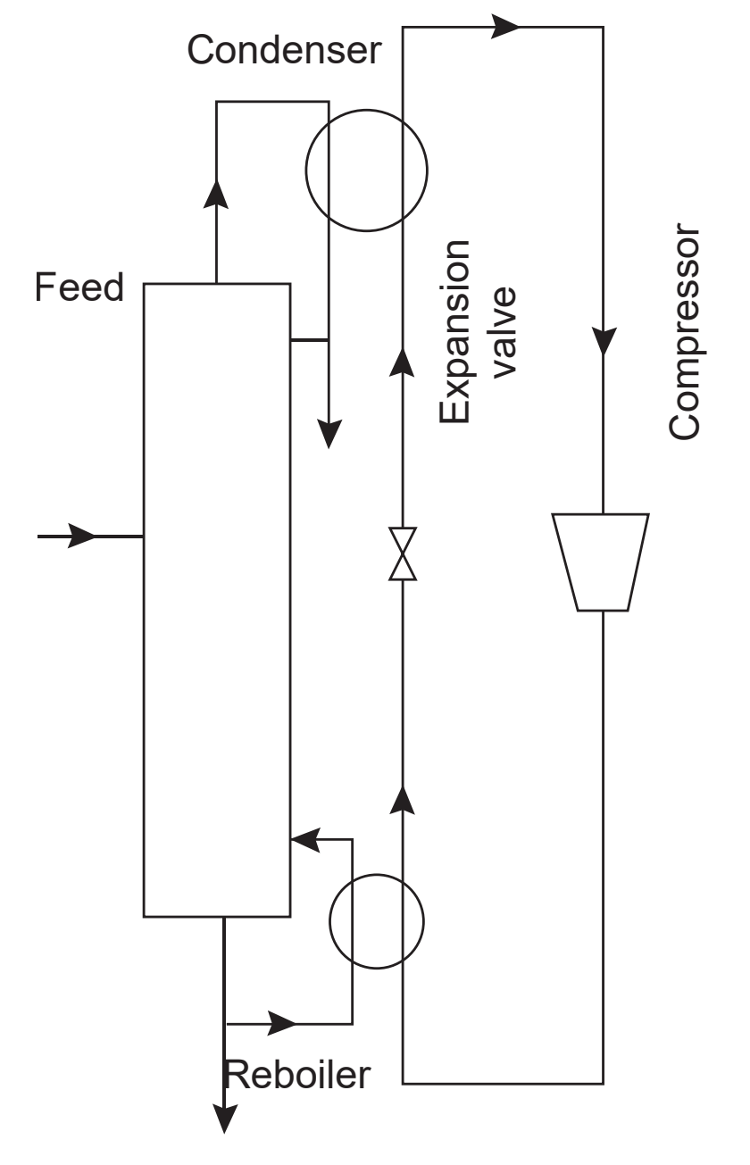


Figure 2: Heat pump integration[1]

Sustainability Advancements

Energy: Combined 96.64 MW managed by 3.64 MW compressor

- Purchase electricity for 3.64 MW instead of 96.64 MW of cooling water and steam

COP: 13.73 out of theoretical 37.12 (37% efficient)

- Assumes a polytropic efficiency of 75%

Economics: $2.25 million annual vs $15.76 million for utilities

- Capital investment of $19.01 million upfront
- Savings of $81.89 million over 20-year project life cycle

Project 2: Sustainable HA Production

Concept of Operations

Project Overview

The project focuses on the largescale production of hyaluronic acid (HA) using biofermentation of *Streptococcus zooepidemicus*. The process includes upstream fermentation, downstream purification, and solvent recovery, with added sustainability features such as combined heat integration, and isopropanol (IPA) recycling. The goal is to produce high molecular weight HA for cosmetic and medical applications while improving process efficiency, reducing environmental impact, and maintaining product quality.

Current Status

Hyaluronic acid is produced industrially via microbial fermentation, with growing demand in pharmaceutical and cosmetic applications. The proposed process integrates fermentation, purification, and solvent recovery, while complying with FDA and GMP standards and environmental regulations.

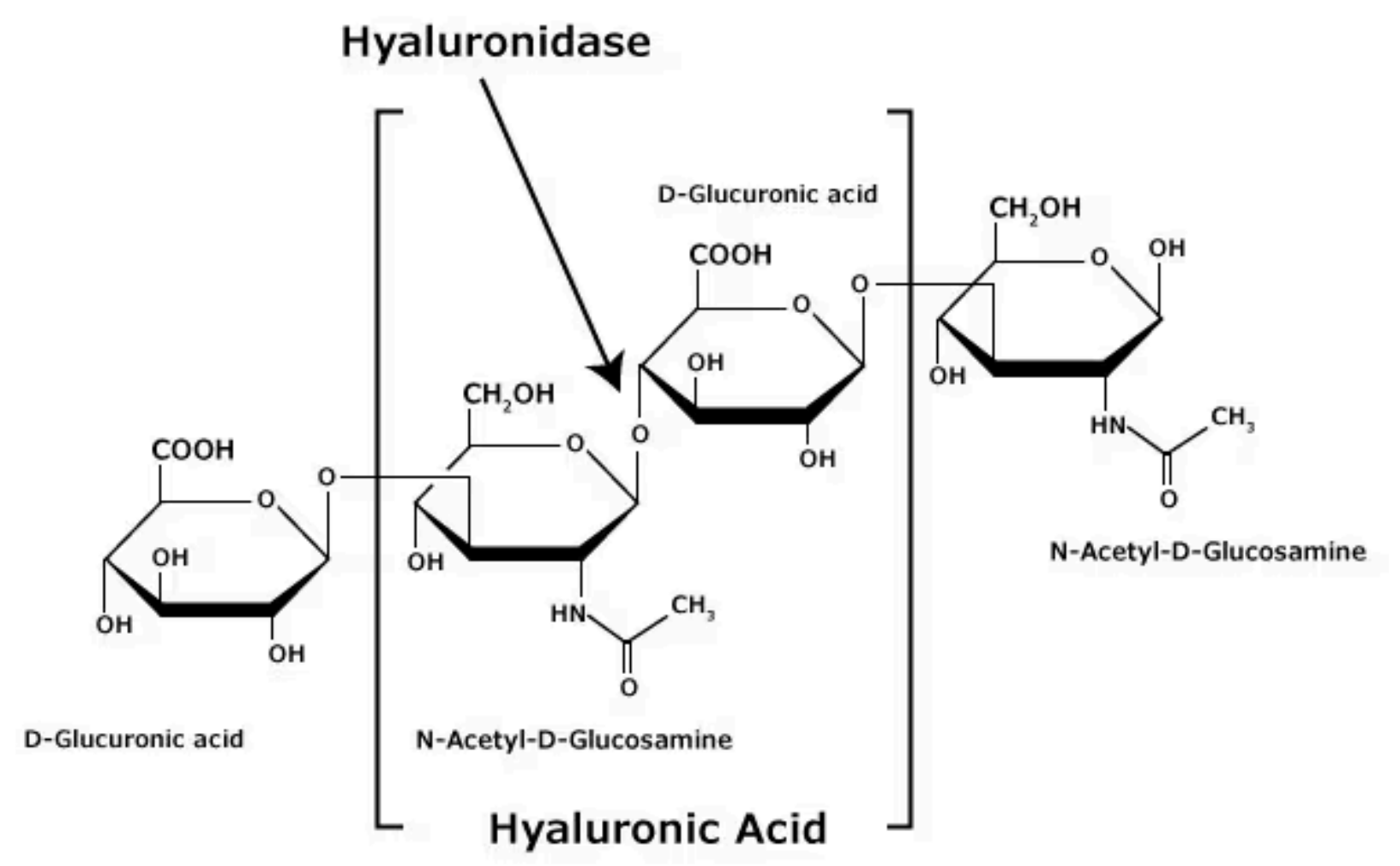


Figure 3: Hyaluronic Acid Structure[2]

Current Deficiencies

- High broth viscosity limits oxygen transfer and mixing
- Competition between cell growth and HA synthesis reduces yield
- Lactic acid accumulation inhibits HA production
- Downstream purification is complex and inefficient
- High energy demand (~5000 kWh per ton HA)
- High water consumption (up to ~10,000 L per batch)

Justification for Change

There is strong demand for high molecular weight HA in medical applications (e.g., ophthalmology and orthopedics). Process improvements are needed to increase yield, reduce energy and water use, and improve sustainability while maintaining product quality.

Operational Scenarios

- Normal operation: continuous fermentation with controlled pH, temperature, and aeration
- Startup/shutdown: gradual system stabilization and controlled flow adjustments
- Upset conditions: contamination, reduced yield, or process instability requiring intervention

Sustainability Metrics

- Economic: production cost, capital investment, ROI
- Carbon: CO_2 emissions from fermentation and utilities
- Water: cooling water and process water demand
- Process: solvent recovery efficiency (IPA recycling)

Separation → Heat Integrated IPA-Water Dist. Column

The highest overall power requirement for our HA manufacture is the distillation column used to separate the IPA and water for IPA recycle. To alleviate this energy demand, the column will be heat integrated in a very similar manner to the Project 1 DIB.

This distillation column consists of:

- Stages: 40
- Total condenser
- Condenser pressure: 1 atm
- Operating Specifications:
    - Distillate rate: 3200 kg/h
    - Reboiler duty: 2000 kW

Distillation results:

- Distillate product:
    - Flow rate: 3200 kg/hr
    - IPA mole fraction: 0.995266
- Bottoms product:
    - Flow rate: 1000 kg/hr
    - H2O mole fraction: 0.9657

Feed Specifications:

- Feed Stage: 25
- Total flow rate: 4200 kg/h
- Temperature: 25 ºC
- Pressure: 1 atm
- Feed composition (mass frac.)
    - 0.786 IPA
    - 0.214 H2O

Power requirements:

- Reboiler duty: 2000 kW
- Condenser duty: -1750.47 kW

Design Concepts

Functional Block Diagram

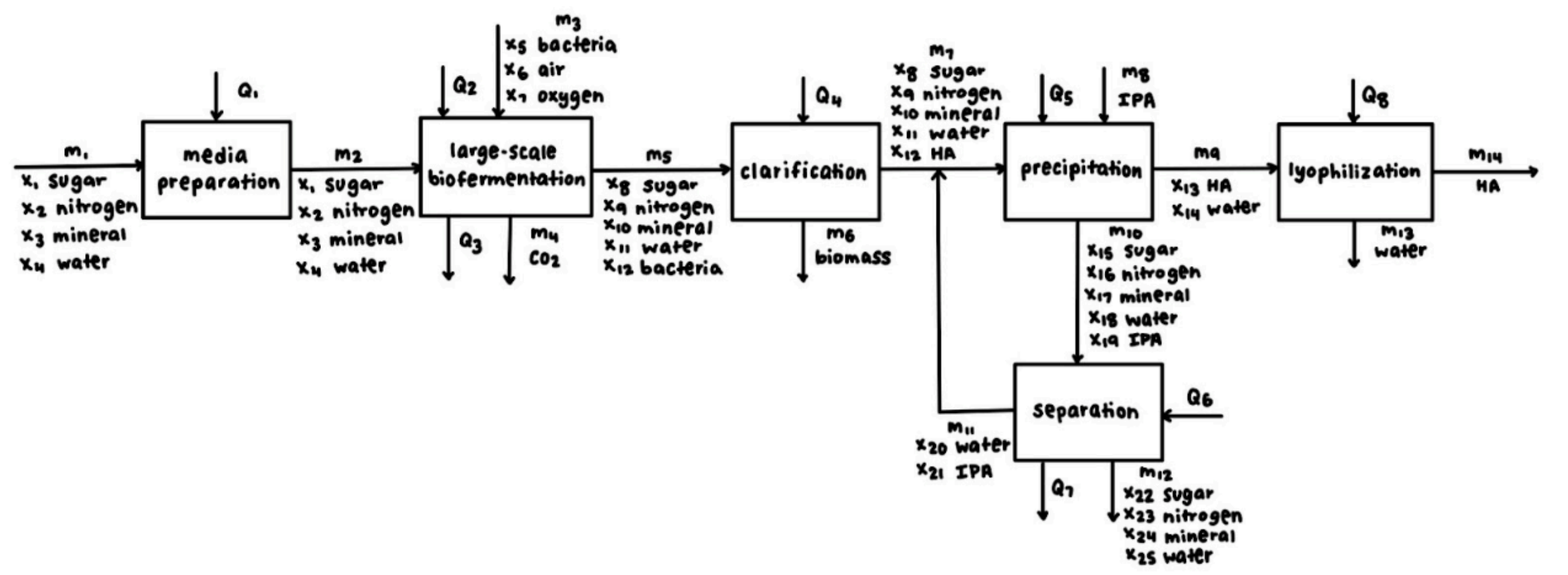


Figure 4: Base case hyaluronic acid manufacture

Example Material and Energy Balances

➔ **Precipitation (Q_5)**

Material balances:

$$m_7(x_8 + x_9 + x_{10} + x_{11} + x_{12}) + m_8 + m_{11}(x_{20} + x_{21}) = m_9(x_{13} + x_{14}) + m_{10}(x_{15} + x_{16} + x_{17} + x_{18} + x_{19})$$

$$x_{20} + x_{21} = 1,\ x_{13} + x_{14} = 1, x_{15} + x_{16} + x_{17} + x_{18} + x_{19} = 1$$

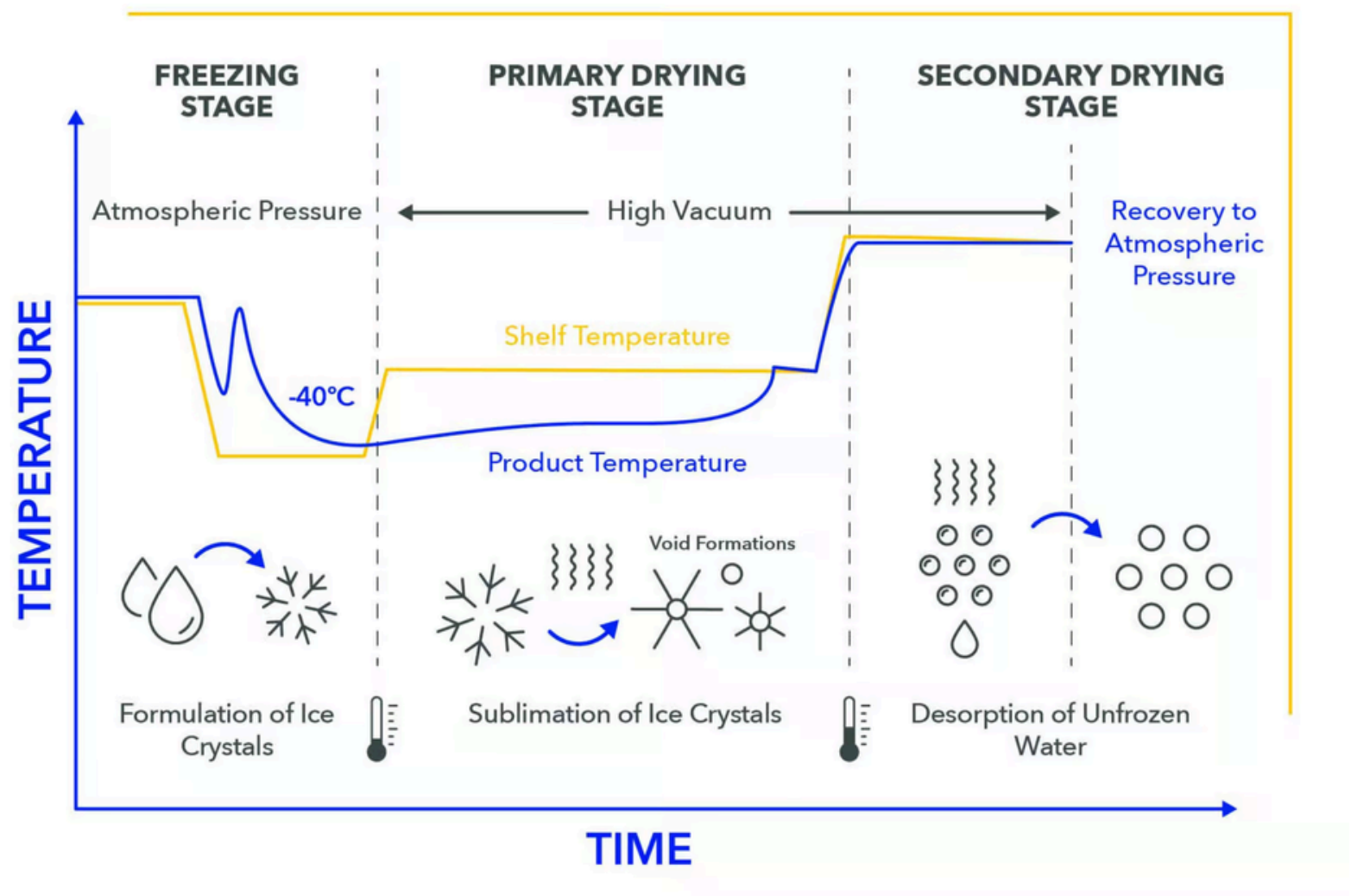
Energy balance:

$$Q_5 = (m_{broth} \cdot C_{p,broth} \cdot \Delta T_{broth}) + (m_{IPA,\,fresh} \cdot C_{p,IPA} \cdot \Delta T_{IPA}) + (m_{IPA,\,recycle} \cdot C_{p,IPA} \cdot \Delta T_{IPA,\,recycle})$$

$$Q_5 = (0.29717\,\tfrac{kg}{s})(4180\,\tfrac{J}{kg\,ºC})(121\,ºC - 25\,ºC) + (0.9169\tfrac{kg}{s})(2680\,\tfrac{J}{kg\,ºC})(25\,ºC - 4\,ºC) + (0.8251\,\tfrac{kg}{s})(2680\,\tfrac{J}{kg\,ºC})(82\,ºC - 4\,ºC)$$

$$Q_5 = 343330\,W = 343.330\,kW$$

Lyophilization Process



There are three main phases in the lyophilization process:

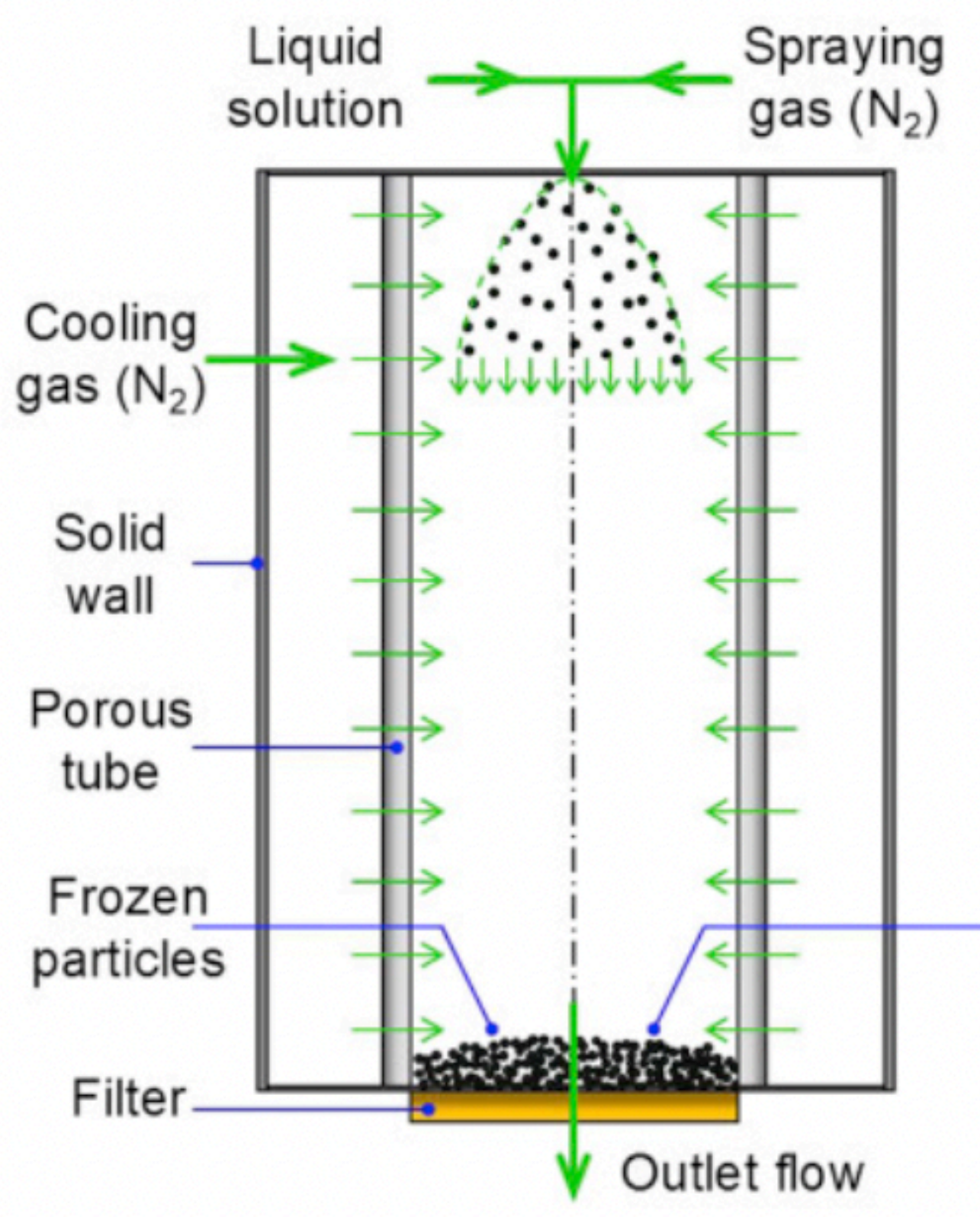
- Phase 1: Freezing (4 hours)
- Phase 2: Primary Drying (24 hours)
- Phase 3: Secondary Drying (8 hours)

This requires a high-powered vacuum system (~100 mTorr) and complex refrigeration (temperatures of -40 to -60 C). This results in a very high specific energy to run the system, at about 10 kWh/kg of product.

Figure 5: Lyophilization process[3]

Alternative Method: Atmospheric Spray Freeze Drying

To combat the high specific energy required of the traditional lyophilization process, our sustainable process will utilize ASFD instead:



ASFD reduces specific energy requirements by 50% compared to lyophilization

The simple process:

- Sterilized HA solution enters a spray nozzle at the top of the cylindrical chamber
- Nozzle atomizes sollution into fine droplets
- The droplets spray downward through cold N_2 gas and freeze
- Frozen particles are collects on a filter at the bottom

Figure 6: Atmospheric Spray Freeze Drying Process[4]

Sustainability Assessment

ASFD (Compared to Lyophilization)

Energy Usage:

- Energy savings of 5 kWh/kg HA.
- Annual energy usage of 89,720 kWh.

Carbon Emissions:

- Emission factor of 0.4 kg CO_2/kWh
- Reduction of approximately 2.0 kg CO_2/kg HA
- Annual production rate of 17,944 kg HA/year
- Annual reduction of 35.9 MT/year.

Water Usage:

- Water savings factor of 0.0075 MT/kWh
- Water savings of 673 MT/year.
- Annual water usage of 29,424 metric tons.

Heat Integration

Energy Usage:

- 3750.14 kW demand reduced to 750 kW (**80% reduction**)
- Balance of compressor power needed with reduced heat requirement of reboiler
- Saving **26.3 million kWh/yr**

Carbon Emissions:

- Annual reduction of 10,512 MT CO_2/yr
- 80% reduction directly proportional to energy usage
- Emissions factor of 0.4 kg CO_2/kWh

Water Usage:

- Savings of 197,100 MT/yr
- Reduces need for steam and cooling water
- Water savings factor estimated as .0075 m^3/kWh

Comprehensive Economic Analysis

- Equipment cost of ~43-54M for ASFD
- **Operation cost lowered by $5.27M/yr**
- Assumes continuous operation with no down time
- Utility rate estimated at $0.20/kWh

Conclusion & Recommendations

Heat pump integration and ASFD enable major reductions in energy usage, CO_2 emissions, and water demand in HA production while maintaining process efficiency. These technologies are recommended for sustainable large-scale implementation. Further improvements can be achieved by optimizing the fermentation process.

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