Cultivating The Future

A Deep Dive Into Cost-Effective Cultivated Meat Production

SuperMeat The Essence of Meat

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Executive Summary

This report details SuperMeat's advancements in establishing a scalable and cost-efficient platform for cultivated meat production. By focusing on 3 key areas - establishing a highly stable cell line with resilience to high shear and low oxygen conditions, fully controlled chemically defined media formulation, and rapid directed differentiation protocols, SuperMeat aims to address the technological challenges associated with large-scale cultivated meat production. This summary highlights the scientific achievements and performance indicators that underscore the platform's ability to support commercially viable cultivated meat production when applied at scale.

High-Density Cell Growth and Rapid Expansion

Optimizing Biomass Accumulation for Efficient Production

SuperMeat's cultivation platform has demonstrated the capability to reach high cell densities, achieving 80 million cells/mL within 9 days of culture. These results reflect the platform's ability to produce substantial biomass in a relatively short time frame, a crucial factor in reaching commercial viability.

Development of a Chemically-Defined, Animal-Component-Free Media (CDM)

Transitioning to Serum-Free Formulations for Greater Consistency and Reduced Costs

SuperMeat has developed a chemically defined media (CDM) to replace traditional serum-based formulations, which are often costly and variable. The CDM eliminates animal-derived components like Fetal Bovine Serum (FBS) and Albumin, addressing both ethical concerns and production inconsistencies. Furthermore, CDM media is superior to lysate-based media, which are usually not well-defined and can pose potential allergen risks. Priced lower than $0.5/L at scale, the f supports high-density cell growth while minimizing the production of byproducts such as lactate and ammonia, thereby maintaining culture health over extended periods.

Efficient Differentiation of Fat and Muscle Tissues

Engineering Cultivated Meat to Mimic Conventional Meat Structures

A key advancement in SuperMeat's technology is the development of differentiation protocols that allow for the production of both fat and muscle tissues in a controlled and rapid process. Fat tissue differentiation is completed in under 24 hours, while muscle tissue differentiation is achieved within 4 days. This approach ensures that the cultivated tissues develop the desired characteristics as conventional meat, while also being suited for scalable production without reliance on scaffold-based systems. Additionally, differentiated cells weigh 1.75 gr/10^9 cells, compared to 1.04 gr/10^9 cells for stem cells, resulting in a significant increase in mass and yield, further enhancing the overall production efficiency.

Continuous Production and Feeding Strategies

Improving Process Efficiency through Optimized Feeding Regimes

SuperMeat demonstrated a continuous production process that integrates both cell

growth and differentiation in a scalable manner. The system uses advanced bioprocess technology to maintain cell density, quality, and metabolic stability over extended periods, demonstrating a consistent supply of high-quality cultivated meat. The process involves a controlled nutrient feeding regime, with a feeding rate of 1.5 VVD on average, and continuous bleeding that sustains cell growth and productivity without compromising culture viability. This approach reduces downtime and allows for the efficient transition of cells from the growth phase to differentiation in an ongoing cycle, further enhancing overall yield and process efficiency.

Path to Scaling and Cost Considerations

Scaling Strategy and Economic Viability

The data collected in the current 10-liter scale production runs provide a foundation for evaluating the economics in larger bioreactors. The continuous production and differentiation processes are structured to be adaptable to large industrial systems, by using well established and proven as scalable equipment and processes, such as full suspension end to end, with Tangential Flow Filtration (TFF) perfusion technology facilitating the sustainment of critical parameters such as cell density, quality, population doubling time, and nutrient management at scale.

Techno-economic analysis of the production system indicates a Cost of Production of $11.8 per pound without depreciation and $13.4 per pound with depreciation when utilizing a 25K scale, within the range of pasture-raised chicken in the US.

The analysis highlights key drivers of production costs that are integral to evaluating the economic feasibility of expanding to larger scales.

These continuous improvements in cellular performance and production cost efficiency demonstrate the potential to achieve scalable and commercially viable cultivated meat production. These developments form a scientific basis for further advancements in the field, aligning with the industry's goals of providing sustainable, nutritious and animal friendly meat.

Background

SuperMeat has pioneered a scalable platform for producing cultivated poultry meat, focusing on utilizing only standard, scalable production processes. Utilizing avian embryonic stem cells (ESCs), coupled with an innovative chemically defined media (CDM), SuperMeat's process is designed to minimize production costs while maintaining high cell densities, quality, and efficient differentiation protocols. This approach is critical for the broader goal of achieving commercial viability in the cultivated meat sector.

Cultivated meat production at scale presents numerous challenges, primarily around controlling costs, optimizing cell growth, and enhancing differentiation capability. SuperMeat's strategy addresses these challenges by implementing a continuous perfusion bioprocess in bioreactors, utilizing standard scalable processes and equipment that have a proven track record of being successfully scaled to full industrial capacity. This report outlines how SuperMeat's technology translates these pilot-scale results into large-scale production, detailing the metrics that drive cost efficiency and scalability.

In the current production setup, SuperMeat has achieved a **Cost of Production of $11.8 per pound** without depreciation, and **$13.4 per pound** with depreciation for 100% cultivated chicken meat, composed of muscle and fat, when applied at 25K liter scale. These costs are competitive with high-end conventional poultry products in the U.S., representing a significant breakthrough for the cultivated meat industry. This cost efficiency is mainly achieved through optimized media usage, fast population doubling times, and innovative differentiation protocols that deliver high yields while supplying product quality and consistency.

SuperMeat's focus on reducing the cost of its animal-component-free media to **below $0.5 per liter**, alongside achieving a cell density of **80 million cells/mL within just 9 days**, highlights the technological advancements that are central to the platform's value. These metrics along with others demonstrate the potential to achieve a commercially viable price for cultivated meat while also showcasing the robustness and consistency of the production process.

SuperMeat's Technology Development: A Commercially Viable Scalable Cultivated Meat Production

SuperMeat has embarked on a development process to create a robust, scalable platform for cultivated meat production. The company's efforts are built upon four key areas of technological advancements, each essential for ensuring a consistent, high-yield production platform: highly resilient cell line, simple and low cost cell feed, high yield continuous production process, and rapid, mass increasing, differentiation protocols. This chapter outlines these advancements, setting the stage for a detailed demonstration of SuperMeat's full production run.

Cell Line Development: Achieving Stability, High Growth, and Consistency

SuperMeat's cell line development focuses on generating robust, high-yield cell clones capable of rapid growth and consistent performance. By establishing a cell line derived from a standard poultry breed (ROSS) and selecting avian embryonic stem cells, SuperMeat ensures that the cells have an innate ability for self-renewal and differentiation into muscle, fat, and other meat tissues.

Clone Development: The process involves a proprietary method for isolating embryonic stem cells from non-incubated, fertilized eggs in an animal-component-free environment maintaining key characteristics that ensure exceptional cell resilience. Following expansion, adaptation for suspension growth, and cloning, the cells become well-suited for large-scale bioreactor processes.

High Growth Rates and Density: The established clones demonstrated stable growth over more than 300 population doublings (PDLs), with cell densities exceeding 20 million cells per milliliter in Erlenmeyer flasks. Additionally, fed-batch experiments demonstrated that SuperMeat's cells have the capability to cycle in under 18 hours, with optimal conditions reducing the cycle time to just 12 hours. These characteristics underscore the clones' potential for achieving high-density cultures in a rapid growth cycle.

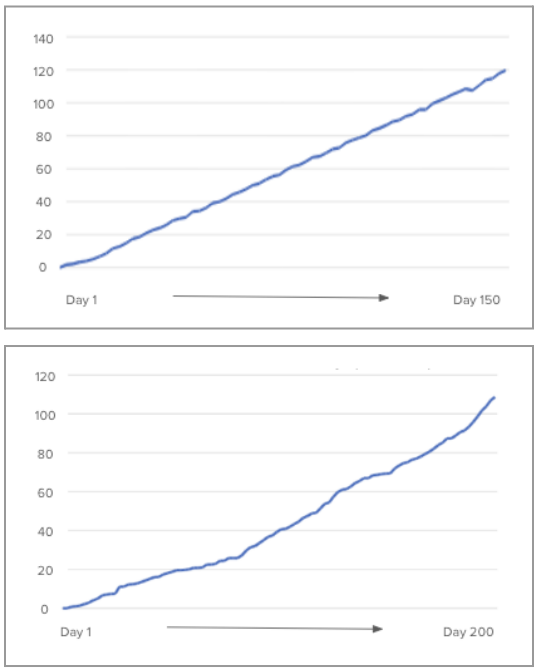

Figure 1: Stability Assessment: PDL Accumulation of Single-Cell Clones Over 150 and 200 Days (Y-axis: Cell Concentration - 10^6 cells/ml)

Stability and Consistency: The clones consistently maintained a stable phenotype, supporting reproducible and long-term production. The rigorous testing of the master and working cell banks (conducted by a third-party contractor, Charles River Laboratories) ensured their suitability for commercial production and alignment with regulatory standards.

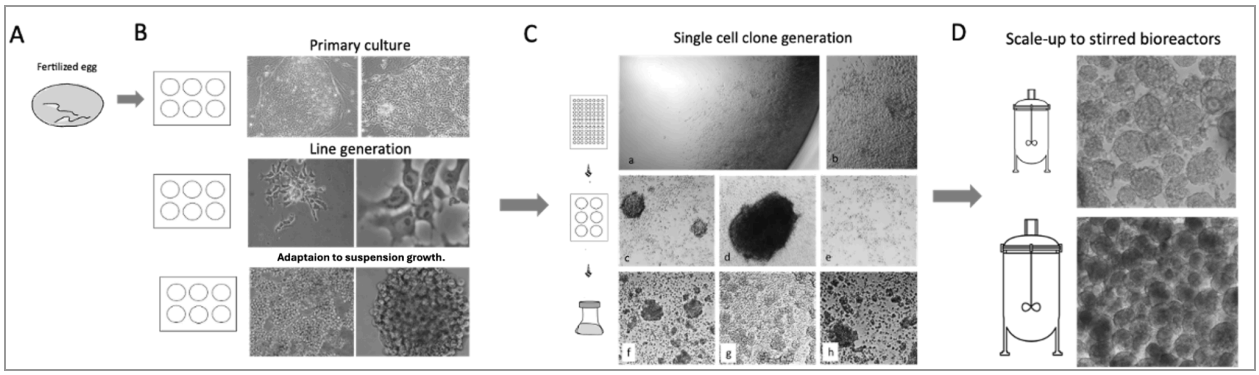

Figure 2: Demonstration of SuperMeat's cultivated meat production: **A.** Process begins with the purification of avian embryonic stem cells from a non-incubated, fertilized chicken egg. **B.** cells are subjected to primary expansion in a cell culture dish. Following expansion, cells undergo adaptation to suspension growth. **C.** following the establishment of suspension-growth primary cell lines, cells are being subjected to single-cell clone generation. Selected clones are used to prepare MCB and WCB for commercial meat production in bioreactors (**D**).

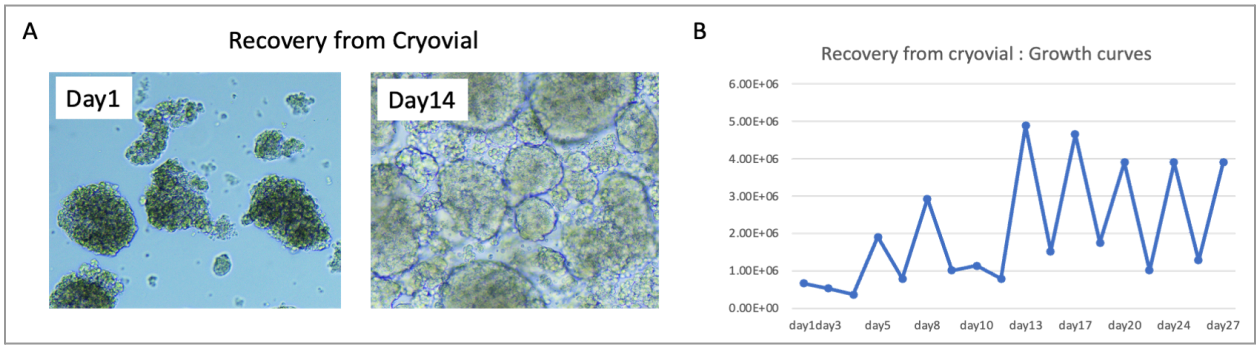

Figure 3: Recovery of cells from WCB cryovials. **A:** Brightfield imaging of thawed WCB ampule (day 1) and same colony after 14 days. **B.** growth curve of a colony that was established from a thawed vial.

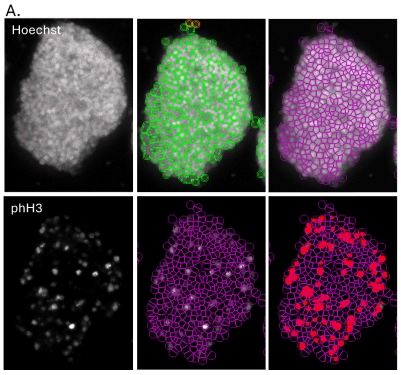

Figure 4: Automated Detection of Proliferative Clones Using the Proliferation Marker pH3

Overview of Media Development: Developing a Chemically Defined Media for Consistent and Scalable Cell Growth

One of SuperMeat's key achievements is the establishment of a chemically defined media (CDM) that supports high-density cell growth without relying on animal-derived components. This serum-free formulation addresses several limitations of traditional media, such as cost, variability, and ethical concerns.

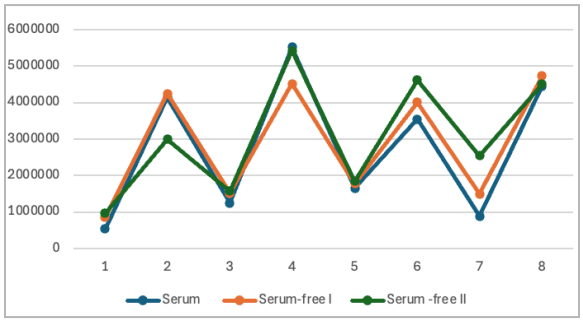

Figure 5: Performance of SuperMeat's CDM Compared with Serum-Based Media (X-axis: Days; Y-axis: Cells/ml)

Optimized Composition: The CDM was formulated with precise concentrations of amino acids, vitamins, growth factors, and trace elements, enhancing nutrient uptake while reducing toxic byproducts such as lactate and ammonia. This targeted approach enables cells to grow efficiently and sustainably in a scalable environment, while also reducing the cost of media to approximately $0.5 per liter when produced at scale.

Comparison to Lysate-Based Media: In comparative studies, SuperMeat's CDM outperformed lysate-based media under critical stress conditions, showing higher cell viability and reduced accumulation of toxic byproducts like ammonia. These results underscore the media's capability to sustain long-term growth and scalability.

Production Process: Mastering Cell Expansion and Metabolic Control for Optimal Culture Performance

SuperMeat's focus on cell expansion involves optimizing both batch and continuous perfusion processes to achieve high cell densities and stable metabolic control, which is essential for efficient cultivated meat production.

Batch Process Optimization: Initial experiments in stirred-tank reactors (STRs) identified optimal conditions for cell growth, including temperature, dissolved oxygen levels, and nutrient consumption. The cells displayed robust growth rates, with a balanced metabolic profile that supported high culture vitality. The STR population was cultured in parallel with samples taken both before and after the bioreactor inoculation.

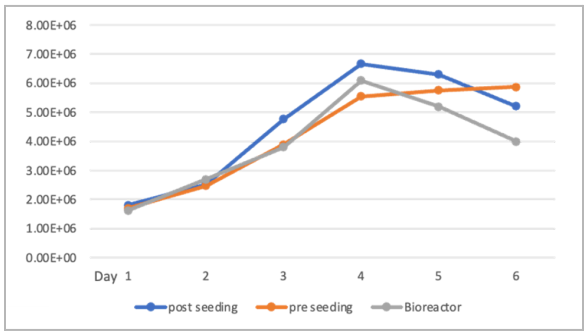

Figure 6: Comparative Growth Dynamics in Bioreactor vs. Pre and post-seeding flasks (cells/ml)

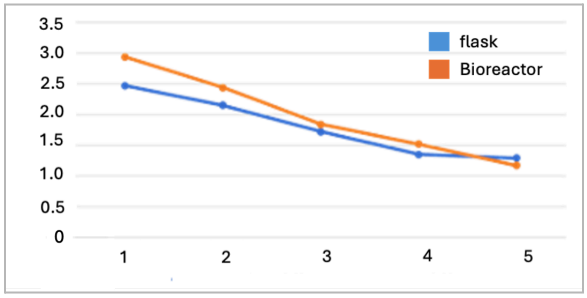

Figure 7: - Glucose Levels (gr/l); X-axis: Day

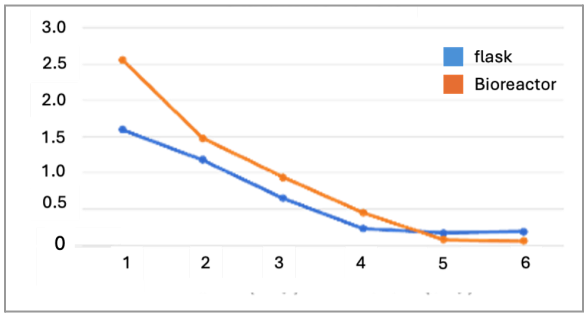

Figure 8: Glutamine Levels (X-axis: Days; Y axis: gr/L)

Implementation of Continuous Perfusion: Transitioning from batch to continuous perfusion allowed for sustained high cell concentrations while maintaining metabolic balance. Using a TFF system and daily bleeding, cell densities reached 40-60 million cells/mL over 25 days, with precise control over nutrient replenishment and waste removal.

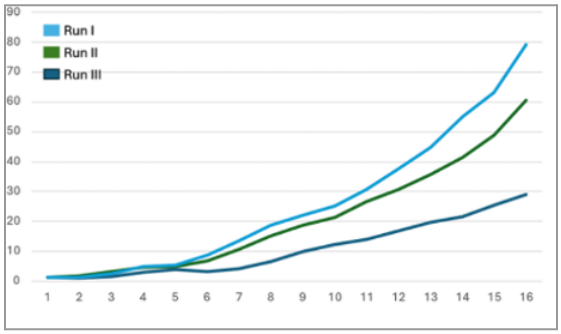

Figure 9: Cell Growth Progression With Optimized Feeding Regime (Cell Concatenation - x10^6 cells/ml, X-axis: Days)

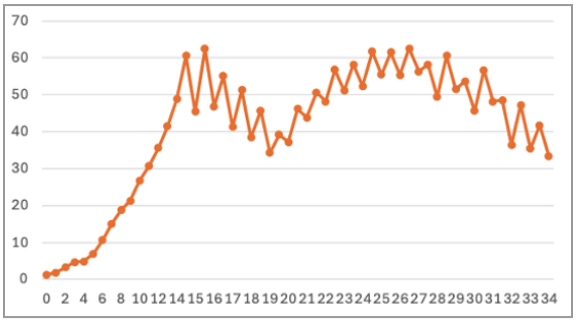

Figure 10: Sustained Concentration During Bleeding Phase (Cell Concentration - x10^6 cells/ml, X-axis: days)

Growth Rate Enhancements: The optimized feeding regime led to cell concentrations of over 80 million cells/mL within 14-15 days, with a population doubling level (PDL) per day of 0.5. Notably, cells were seeded at concentrations of 0.5 million cells/ml, demonstrating remarkable recovery within the bioreactor tank. An improved feeding strategy resulted in achieving the same concentration of 80 million cells/mL with an accelerated growth rate of just 9 days, as will be detailed in the next chapter. This advancement is a critical step toward achieving high productivity in a scalable production setup.

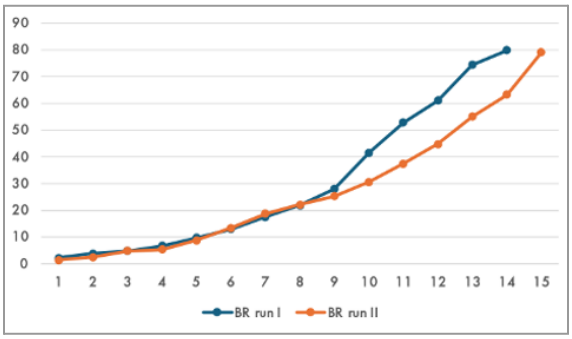

Figure 11: Reproducible High Cell Density in Optimized Continuous Process (Y-axis: Cell Concatenation - x10^6 cells/ml X-axis: Days)

Differentiation Development: From Stem Cells to Meat - Efficient Fat and Muscle Tissue Engineering

SuperMeat's ability to efficiently differentiate its stem cell platform into fat and muscle tissues marks a significant breakthrough in the production of cultivated meat.

The focus on full-suspension, scaffold-free differentiation of muscle enables scalable tissue-like structures that produce the texture, taste, and nutritional qualities of conventional meat.

Scalable Fat Differentiation: SuperMeat's protocol for fat differentiation successfully converts stem cells into mature adipocytes within up to 24

hours, achieving 95-100% differentiation and up to 50% lipid coverage in cell cultures. The process is designed to operate in stirred-tank bioreactors, ensuring scalability and uniform fat production without the need for scaffolds.

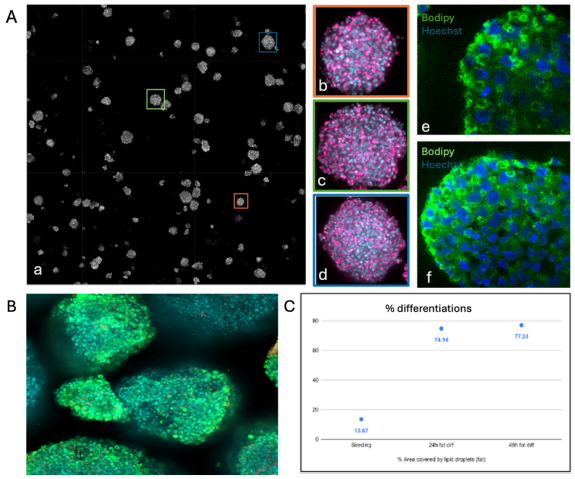

Figure 12: Reproducibility of Lipid Production in Bioreactors

Muscle Differentiation in Suspension: Achieving muscle differentiation without scaffolds is a complex challenge. SuperMeat has established a protocol that induces muscle fiber formation within 4 days by guiding cell clusters to self-align, promoting a natural 3D structure. The resulting muscle cells exhibit key characteristics of conventional meat, including the expression of myosin heavy chain and enhanced protein synthesis.

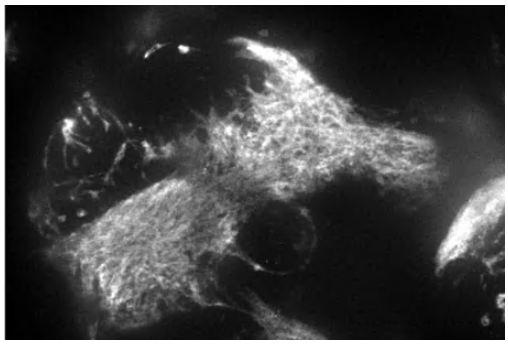

Figure 13: Immunostaining Confirmation of Myosin Heavy Chain Expression in Myotubes

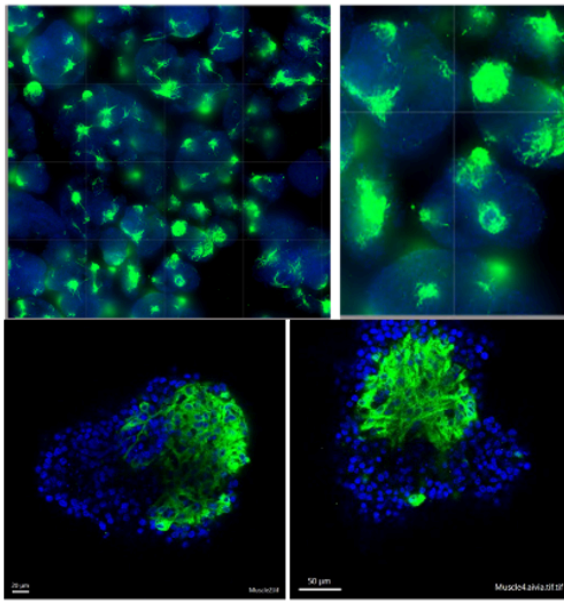

Figure 14: 3D Alignment of Muscle Fibers Free of Artificial Scaffolds (Bar graph - 50um)

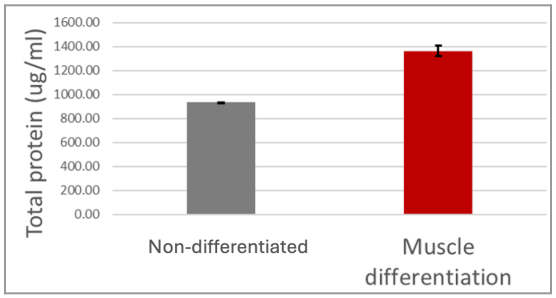

Figure 15: Total Protein Content (ugr/ml) in Differentiated Muscle Compared to Stem Cells (Non-Differentiated)

Integration of Fat and Muscle Production: The continuous differentiation process supports the simultaneous production of fat and muscle tissues, with cell densities reaching up to 80 million cells/mL. This integrated approach allows for the seamless transition from cell expansion to tissue production, maximizing yield and reducing production time.

Conclusion

SuperMeat's comprehensive technology has established a strong foundation for scalable and efficient cultivated meat production. By

establishing a powerful cell line platform, tailored chemically defined media, robust cell expansion process, and rapid tissue differentiation protocols, the platform supports a high yield efficient manufacturing process.

Demonstrating an End-to-End Cultivated Meat Production Technology

The previous chapter described the development of SuperMeat's production platform, which includes tailored cell feed formulations, scalable bioprocess innovations, and continuous process improvements. This chapter brings together these elements into a cohesive cultivated meat production run, highlighting the integration of seed-train preparation, rapid cell expansion, differentiation, and key properties of the resulting cell mass.

This comprehensive production run allowed to demonstrate different feeding regimes, optimized yields, and demonstrate the process's performance for future commercial applications. The findings from these production runs also provide data points for the techno-economic model.

Complete Production Run Overview

The production run was carried out using a continuous setup, beginning with a 2L bioreactor for inoculum preparation, followed by a 10L bioreactor for cell expansion, and concluding with two 10L bioreactors for differentiation into muscle and fat tissues. This integrated approach enabled us to demonstrate the scalability and reproducibility of the production platform. Over several cycles of differentiation into fat and muscle tissues, the production run demonstrated a consistent high cell density achievement.

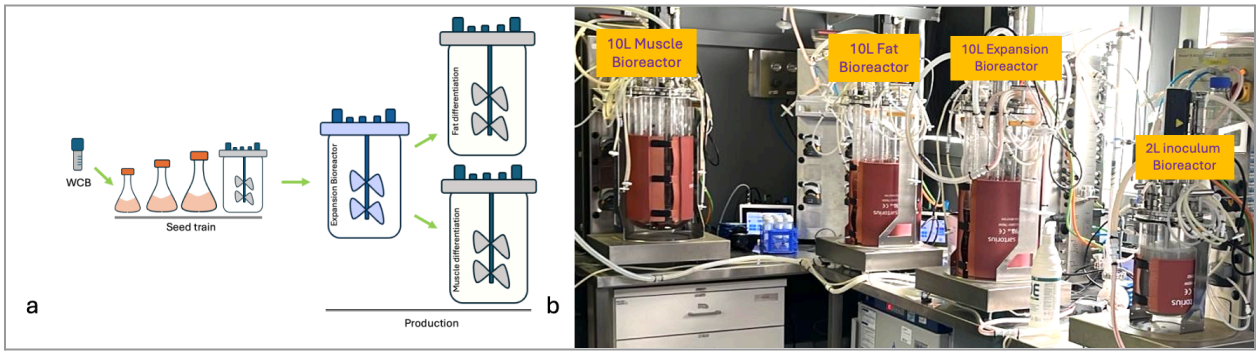

Figure 16: Schematic Overview of the Complete Cultivated Meat Production Line

Inoculum Preparation

The inoculum preparation phase began with the thawing and expansion of the working cell bank in Erlenmeyer flasks, which allowed for the growth of cells to densities necessary for inoculation into larger bioreactors.

Cell Expansion Dynamics: Cells were expanded from a starting concentration of 0.5-0.7 million cells/mL to over 40 million cells/mL in the 2L bioreactor. During this process, cell proliferation rates ranged from 0.3 to 0.7 PDL/day, with stable consumption of glucose, glutamine, and pyruvate, alongside moderate lactate and NH_4^+ formation.

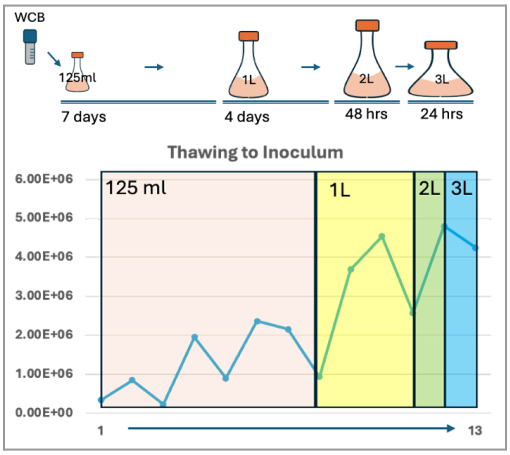

Figure 17: Inoculum Seed Train

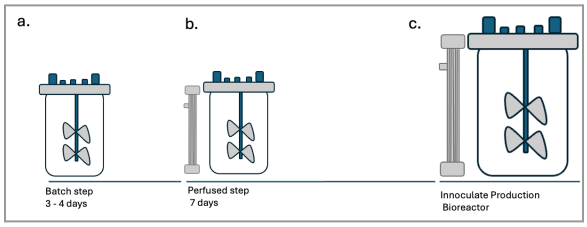

Figure 18: Inoculum Preparation Scheme

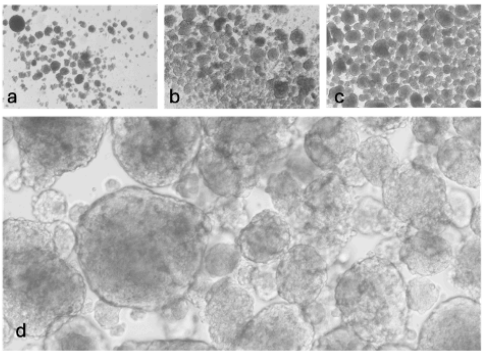

Figure 19: Microscopic and Phenotypic Observation of Cell Expansion in Seed Train. A: 24 hrs post thawing. B-D: inoculum expansion over a 12 day period.

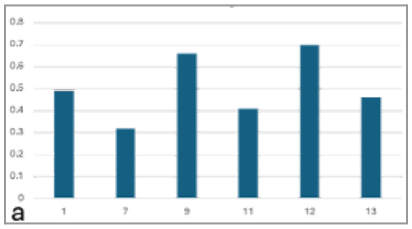

Figure 20: Seed-Train Flask Growth Rate (Axis -X: Days; Axis-Y: PDL)

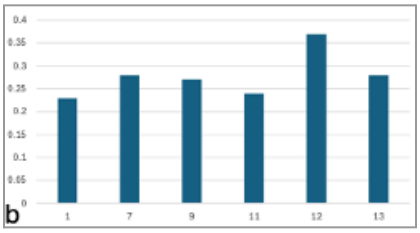

Figure 21: Glutamine Consumption Rate (Axis -X: Days; Axis-Y: gr/L)

Metabolic Analysis: Metabolic profiles revealed balanced energy production cycles, with glucose and glutamine consumption accelerating from day 4 of the expansion phase, indicating robust cellular activity. NH_3 levels remained controlled, keeping under 0.7 mM through media perfusion adjustments.

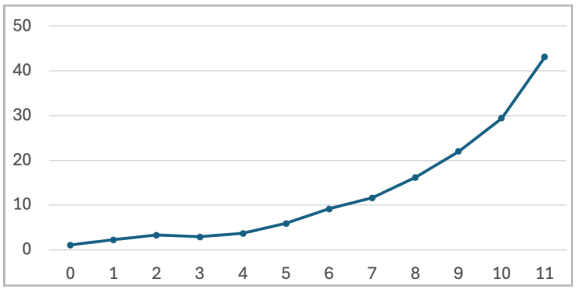

Figure 22: Growth Curve of Inoculum Preparation in 2L Bioreactor (Cell Concatenation - x10^6 cells/ml; X-axis: days)

Figure 23: Performance of Expanded Inoculum in 2L Bioreactor (Axis X for all graphs - Days)

Expansion Bioreactor Performance

The expansion bioreactor was seeded with an initial concentration of 5 million cells/mL, facilitating the achievement of high cell densities within a short time suitable for subsequent differentiation into fat and muscle tissues.

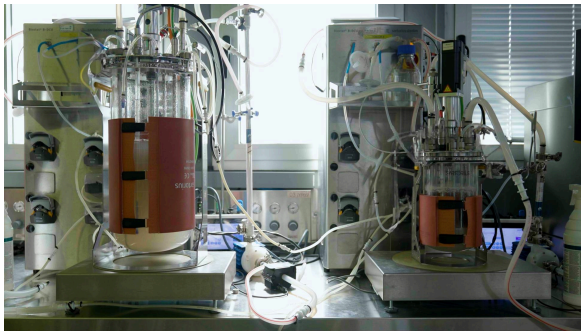

Figure 24: 10L Bioreactor Seeding

Figure 25: 10L Bioreactors During Cell Expansion Phase

Perfusion System Integration: The bioreactor was connected to a TFF system to manage nutrient supply and waste removal, achieving an optimal balance between nutrient replenishment and cell growth. Perfusion rates increased from 1 VVD to 5 VVD, maintaining high cell densities. The goal is to achieve high densities that allow bleeding while maintaining an average perfusion rate of 1.5 VVD throughout the process.

High-Density Culture Achievement: In 9 days, the culture reached a density of 80 million cells/mL, with cells growing at an average rate of 0.52 PDL/day.

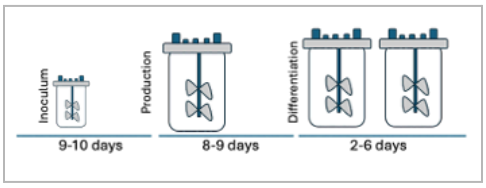

Figure 26: Schematic Overview of Expansion Stage

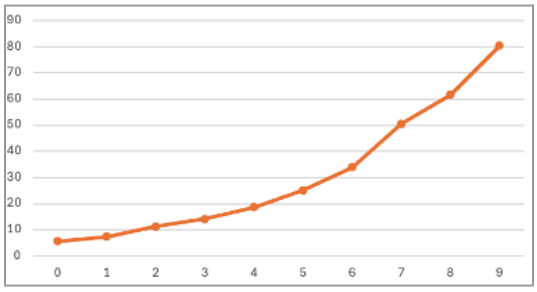

Figure 27: Cell Densities in 10L Bioreactor (Axis-Y: x10^6 Cells/mL; Axis-X: Days)

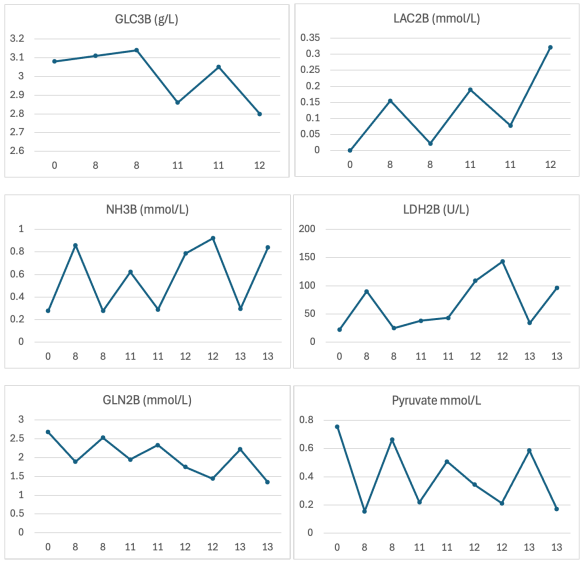

Figure 28: Metabolic Analysis Showing Glucose, Glutamine, and NH_3 Levels During Inoculum Expansion

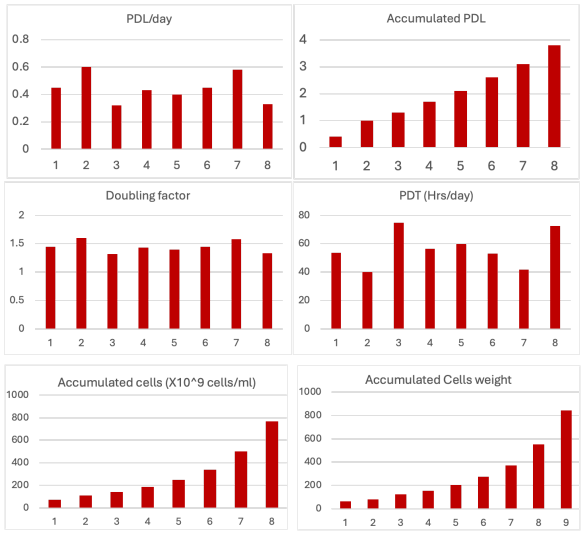

Figure 29: Cell Performance in a 10L Bioreactor (Axis-X: Days; Y-Axis for Cell Weight - grams)

Figure 30: Daily Sample for Monitoring and Control

Demonstration of Feeding Regimes

Two different feeding regimes were demonstrated during the production run to optimize the cost-efficiency and productivity of the process. The goal was to reduce media exchange rates while maintaining high cell densities.

Implementation of production Feeding Regime: The production feeding regime strategy, applied prior to the muscle differentiation phase, reduced the average media exchanges to 1.5 volume per day while increasing cell concentration.

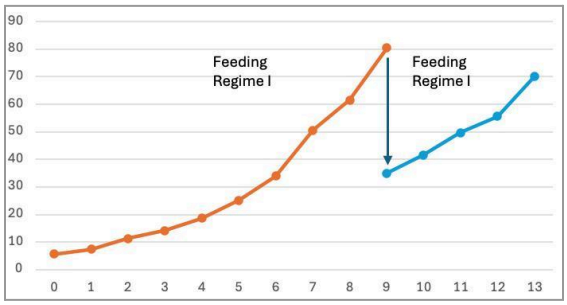

Figure 31: Cell Concentration & Growth Rates Under Different Feeding Regimes in Bioreactor - Average 2.5 VVD (Orange) vs. 1.2 VVD (Blue), x10^6 Cells/mL

Metabolic Stability: The new regime showed a lower glucose consumption rate compared to the original formula, with significantly reduced lactate production. Pyruvate consumption was directly linked to the TFF filter flux rate adjustments, suggesting enhanced metabolic activity and energy production.

Figure 34: Cell Feed Preparation

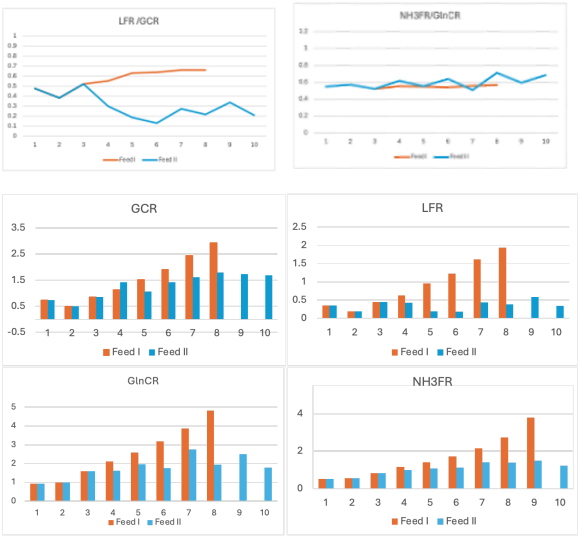

Figure 32 - Metabolic Analysis of Key Metabolized Formation And Consumption (Feeding regimen with an average of 2.5 VVD (orange) compared to an average of 1.2 VVD (blue)

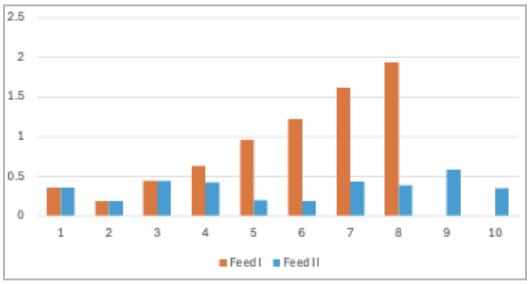

Figure 33: Metabolic Efficiency of Feeding Regimes in Reducing Lactate Production (Lactate Formation Rate) compared to the old feed type

Figure 35: Cell Feed Bag

Directed Differentiation into Fat and Muscle Tissues

The final step in the production process involved transferring the expanded cells into differentiation bioreactors to induce the formation of fat and muscle tissues.

Fat Differentiation: Cells were transitioned to the fat differentiation bioreactor at a concentration of 40 million cells/mL. 24 hours post differentiation induction, the cells showed extensive lipid droplet accumulation and a shift to a white pellet color, consistent with conventional chicken fat.

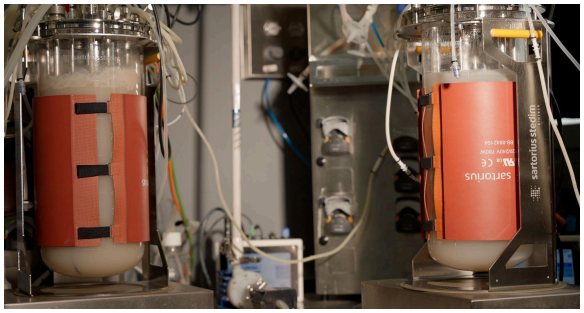

Figure 36: 10L Bioreactor During Differentiation Phase

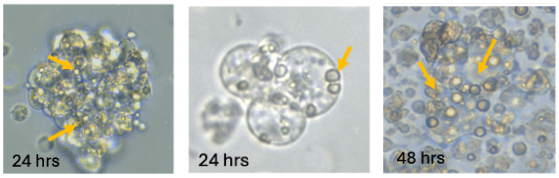

Figure 37: Lipid Droplet accumulation in Differentiated Fat Tissue

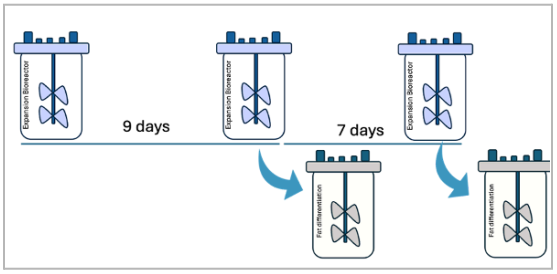

Figure 38: Scheme of Fat Differentiation Process

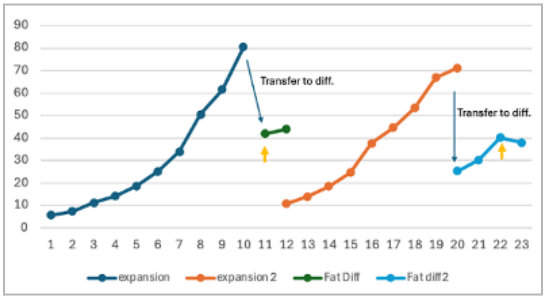

Figure 39: Reproducibility of Cell Growth and Concentrations Following Bleeding and Transfer to Fat Differentiation Bioreactor (Axis-Y: Cell Concentration - x10^6 Cells/mL; Axis X - Days)

Figure 40: Comparison of Differentiated (Fat) Cells vs. Non-Differentiated Biomass

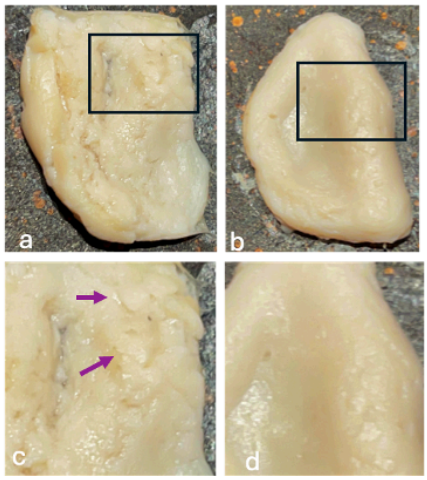

Figure 41: Comparison of Fat Tissue vs. Non-Differentiated Biomass (A & C: Fat; B & D: Non-Differentiated)

Muscle Differentiation: Pre-muscle differentiation, the bioreactor culture was expanded to a density of 70-80 million cells/mL. The differentiation process lasted 4 days, resulting in the production of muscle fibers that closely resembled ground chicken meat in both appearance and texture.

Mass Increase During Differentiation: During the differentiation process, cells undergo significant phenotypic and physiological changes, leading to an increase in diameter (from approximately 12 µm to 16 µm) and a corresponding increase in volume of about 2-fold.

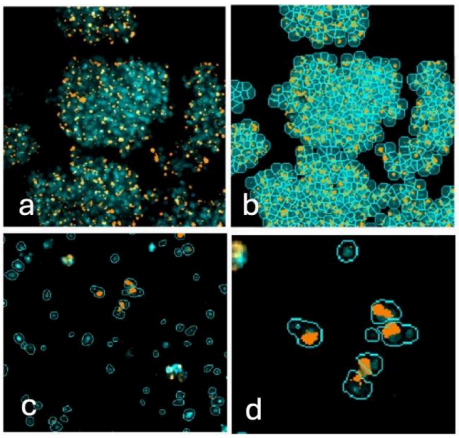

Figure 42: Automated High-Throughput Image-Based Analysis of Fat-Differentiated Cells with Single-Cell Identification and Automated Volume and Size Quantification

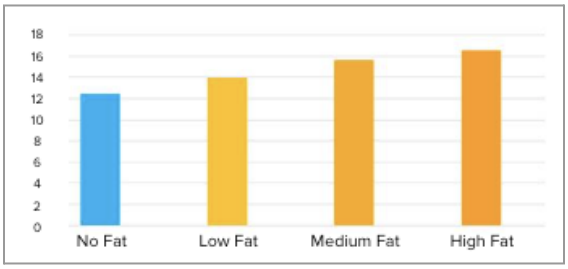

Figure 43: Cell Diameter (µm)

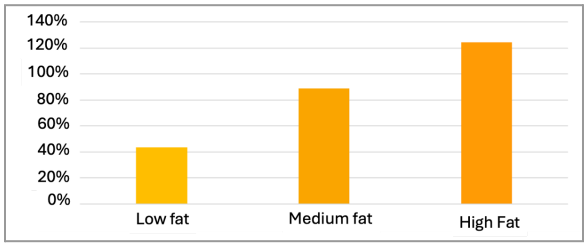

Figure 44: Cell Volume Increase (%)

A High-Yield Production Platform

In the SuperMeat production process, the yield is enhanced by the cells' ability to sustain a 30% bleeding rate during the 45-day bleeding phase,

combined with rapid differentiation that increases the overall biomass. Following the initial 9-day growth period, and the 45-day bleeding phase the production process yields approximately 33 kg of biomass. The process is supported by one primary 10L bioreactor for cell expansion and two additional 10L for the differentiation processes. A total of 945 liters of media is required to generate the 33 kg yield. Differentiation takes 2 days on average, with an additional 3 days until differentiation bioreactors are filled and the process begins. On average, 7-8 lots (harvests from each differentiation bioreactor) are produced throughout the 45-day continuous process, resulting in a steady output of cultivated meat.

Figure 45: Cultivated Meat - Minced (85% Muscle & 15% Fat)

Figure 46: Pre-Cooked Cultivated Chicken Patties (100% Cultivated Meat)

Figure 47: Grilled Cultivated Chicken Burger Patties (100% Cultivated Meat)

Summary

The comprehensive production run demonstrates the key advancements of SuperMeat's cultivated meat platform, showcasing high cell densities and rapid and efficient differentiation protocols into fat and muscle tissues that facilitate a high yield commercial cultivated meat manufacturing system.

Techno-Economic Analysis of SuperMeat's Cultivated Poultry Meat Production at an Industrial Setting

Introduction

This Techno-Economic Analysis (TEA) explores the cost efficiency and scalability of SuperMeat's cultivated poultry meat production process. extrapolating on data collected from SuperMeat's 10-liter production runs, this analysis evaluates the potential to reach commercial viability in a 25,000-liter production facility with 5 production lines.

Key parameters such as media usage, cell growth, differentiation capability, energy usage, and other parameters are thoroughly examined to provide insights into the factors influencing the cost per pound (COGs) of cultivated meat production. The sensitivity analysis identifies which variables most significantly impact economic viability, offering actionable insights for further improvement as SuperMeat advances towards large-scale production.

Further optimizations are in progress, including media enhancement, refined feeding strategies, and process parameter improvements. Combined with economies of scale and increased operational efficiencies, these efforts will significantly drive down costs in the following years, facilitating further cost reduction to cost competitiveness with commodity poultry products.

Methodology and Key Parameters

The analysis is grounded in assumptions that reflect SuperMeat's current production parameters, scaled to an industrial facility. Key parameters include:

- Facility Size: 25,000-liter scale (Refer to the explanation below for the rationale behind selecting the 25,000L facility in the Techno-Economic model).
- Number of Production Lines: 5
- Rejection Rate: 3%
- Cell Viability at Seeding: 95%
- Cell Concentration During Bleeding Phase: 80 million cells/ml
- Cell Doubling Time During Bleeding Phase: 0.5 PDL/day.
- Bleeding Rate: 0.35 VVD.
- Continuous Process Duration: 45 days. SuperMeat's platform has demonstrated continuous bleeding for extended periods of times as well as clonal stability tests for over 300 PDLs.
- Differentiation Time: 2 days (fat differentiation <1 day; muscle differentiation 4 days).
- Cell Wet Weight: Stem cells: 1.04 gr/10^9 cells; Mature cells: 1.75 gr/10^9 cells
- Energy Cost: $0.08/kWh
- Media Cost and Usage: <$0.5 per liter, and a media feeding rate of 1.5 VVD during bleeding phase.
- Differentiation media: <0.5$/L.
- Media: Chemically defined media, concentrated 10 fold and diluted on line when introduced into the bioreactor (Use of concentrated media saves energy for cooling and heating, media storage vessels and manpower for media handling).
- Bioreactor Assembly Time: 6 days.
- Labor: 100 full-time employees; 13 outsourced positions.

Rationale Behind the 25,000L Facility Choice in the Techno-Economic Model

The decision to base the techno-economic model on a 25,000-liter bioreactor facility is informed by established practices in industrial biotechnology and the proven scalability of similar systems. Facilities of this size are widely employed in animal cell culture processes, as outlined by Hans-Peter Meyer, Wolfgang Minas, and Diego Schmidhalter in *Industrial-Scale Fermentation, Industrial Biotechnology: Products and Processes* (First Edition, Wiley-VCH Verlag GmbH & Co. KGaA, 2017). Large-scale bioreactor operations are active in several regions, including the US (e.g., Roche in California), Europe (e.g., Diosynth Biotechnologies in Denmark, Merck in Switzerland), and Asia (e.g., Lonza Biologics in Singapore). SuperMeat's production process utilizes full suspension, similar to the methods used in the referenced facilities. The cells demonstrate high resilience to shear stress, minimal heat generation during growth, while the perfusion system is designed for scalability. These factors make scaling up to a 25,000L bioreactors highly viable, supporting large-scale cultivated meat production.

Engineering Solutions for Scale-Up: Cell Resilience and System Optimization:

1. Shear Resistance of Cells: One of the key technical challenges in scaling up is managing the shear stress that cells experience due to high agitation rates in large-scale systems. SuperMeat's stem cells have demonstrated robustness under high shear conditions in 10L and 200L bioreactors, successfully operating at high agitation with a combination of Rushton and pitched blade impellers. These conditions, with a power input of 62 W/m^3 and a tip speed of 1.1 m/s, indicate that SuperMeat's cell lines can sustain the mechanical stress encountered in larger bioreactor systems, supporting their suitability for scale-up.

2. Temperature Control and Heat Management: Temperature regulation is another critical aspect of large-scale operations, as cell metabolism generates heat that must be efficiently dissipated. Stem cells generally exhibit lower heat production compared to other cell types, as noted by Meyer et al., 2017. This reduced thermal load minimizes the energy required for cooling, thereby simplifying temperature control in a 25,000L bioreactor setting.

3. Media Management: Using 10-fold concentrated media with in-line dilution will streamline media preparation, reduce the need for large media holding tanks, and lower energy consumption for media heating.

4. Staged Scale-Up Strategy: SuperMeat leverages Computational Fluid Dynamics (CFD) simulations to optimize this process, allowing us to predict and control key parameters such as fluid dynamics and nutrient distribution. CFD tools are instrumental in ensuring that the physical and engineering aspects of the scale-up process are precisely managed.

Production Metrics and Results

These baseline parameters above set the context for the sensitivity analyses and COGs projections provided below.

Assuming continuous operation in an industrial facility (25,000 liters), SuperMeat's production capacity and costs have been calculated based on these assumptions.

- COGS: $11.8 per pound (without depreciation) and $13.4 per pound (with depreciation). Within the range of pasture-raised chicken in the US[1].
- Annual Production Volume: 6.7 million pounds, equivalent to the meat of approximately 2.7 million chickens, or 13.4 million individual chicken breasts.
- Production Cycles: 5.7 cycles per year of each expansion bioreactor (28.5 batches a year for all 5 production lines), yielding 472.9 lots annually (each lot represents a single harvest from a differentiation bioreactor).
- Media Usage: 92,772K liters per year.

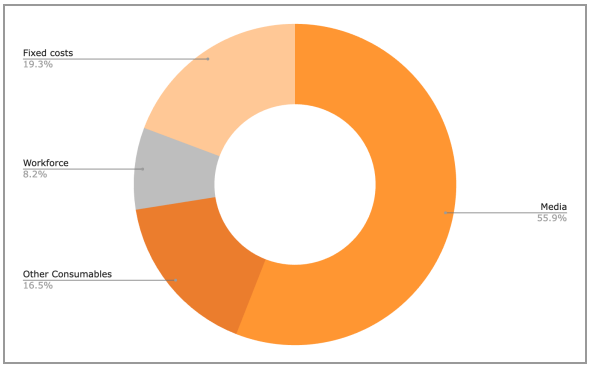

Figure 48: COGS Distribution (%)

Process Description

As outlined in the previous section, SuperMeat has developed a production process initially optimized in 10L bioreactors. The industrial-scale production will be scaled up to 25,000L bioreactors.

The process begins with the thawing of one or more ampoules from the working cell bank in the CDM medium, followed by cell propagation in Erlenmeyer flasks. These flasks are maintained in a shaker incubator. Subsequent cell propagation occurs in seed-train bioreactors. The final stage of the seed train takes place in a 5,000L bioreactor, where cells undergo perfusion to achieve a high-density culture.

The cell culture from the 5,000L seed bioreactor is then used to inoculate the 25,000L expansion bioreactor. During this stage, cell growth is conducted in perfusion mode utilizing a TFF system to optimize cell growth by continually replacing the spent media with fresh media. Once the cell culture reaches a density of approximately 80 million cells/mL, a continuous bleeding process begins, lasting 45 days.

Cells are continuously transferred into the 25,000L differentiation bioreactor, where the media is replaced with differentiation media using the TFF system. Differentiated cells, either fat or muscle, are harvested and collected, with the resulting cell pellet stored at -20°C.

Media Use and Cost

At scale, the media cost is estimated at below $0.5 per liter, reflecting the current media composition and future volume purchasing from SuperMeat's suppliers. With an average media exchange rate of 1.5 VVD during the bleeding phase (a controlled extraction of a portion of the cell biomass before transferring it to a sequential bioreactor for the differentiation process), further optimization of media usage will be required for further lowering cost.

[1] https://usda.library.cornell.edu/concern/publications/cj82kn551?locale=en

	Media Exchange rate (VVD)						
Media Cost ($/L)	1.00	1.25	1.50	2.00	2.50	3.00	4.00
0.3	9.82	10.35	11.03	12.09	13.15	14.21	16.49
0.4	10.79	11.41	12.23	13.48	14.74	16.00	18.70
0.5	11.75	12.48	**13.42**	14.88	16.33	17.79	20.92
0.6	12.71	13.54	14.61	16.27	17.92	19.57	23.13
0.7	13.67	14.60	15.81	17.66	19.51	21.36	25.35
0.8	14.64	15.66	17.00	19.05	21.10	23.15	27.56

Table 1: Sensitivity Table - Impact of Media Cost per Liter and Media Usage (daily media exchange rate, VVD) on COGs (US$/lbs).

Population Doubling Time (PDT) and Cell Concentration

The target cell concentration of 80 million cells/ml was reached in 9 days, and maintained throughout the bleeding phase.

The average Population Doubling Time (PDT), which indicates the cells' growth rate, is 0.67 PDL during the propagation phase, extending to 0.6 and 0.5 PDL during the perfusion and bleeding phases, respectively. A rapid growth phase is essential for generating sufficient biomass in a short timeframe. Attaining the desired concentration efficiently minimizes media usage, energy consumption, and bioreactor time, all of which keep production costs low.

Given the extended duration of the bleeding phase, SuperMeat assessed the impact of PDT during this stage, along with the target cell density, on the COGS.

	Cell Doubling time during bleeding (PDT, Hours)							
Cell Density (10^6/ml)	25	30	35	40	48	55	60	70
50	16.29	17.43	18.38	19.32	20.80	22.07	22.97	24.73
60	13.66	14.61	15.41	16.20	17.45	18.53	19.29	20.78
70	11.78	12.58	13.28	13.96	15.05	15.98	16.64	17.94
80	10.36	11.05	11.67	12.28	**13.42**	14.06	14.64	15.79
90	9.24	9.86	10.41	10.96	11.82	12.56	13.08	14.11
100	8.35	8.90	9.40	9.90	10.68	11.35	11.83	12.76

Table 2: Sensitivity Table - Impact of cell doubling time and cell concentration on COGs (US$/lbs).

Differentiation Process

SuperMeat's process maximizes biomass yield through differentiation. The average differentiation duration is 2 days, with fat and muscle differentiation times varying. Differentiated cells weigh 1.75 gr/10^9 cells, compared to 1.04 gr/10^9 cells for stem cells, which substantially impacts yield and cost.

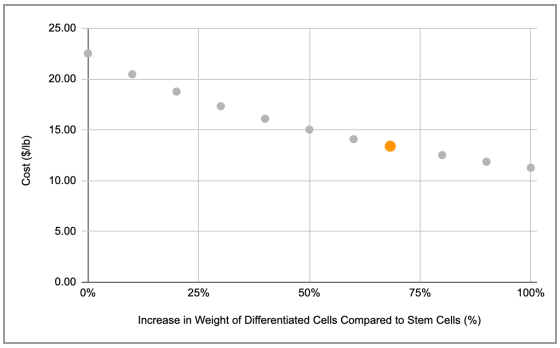

Figure 49: Effect of the Percentage Increase in Differentiated Cell Weight Compared to Stem Cell Weight on COGs ($/lb)

Production Metrics

The production phase lasts for **45 days**, during which cells are harvested (bleeding phase) and then transferred to the differentiation stage, within a total production cycle time of 56.3 days from seeding to final harvest, yielding **5.7 cycles per year**, and producing **472.9 lots per year**.

Each lot represents a single harvest from a differentiation bioreactor, while a full cycle includes the entire expansion process. With **28.5 batches per year**, the facility is designed for high throughput and minimal downtime between batches.

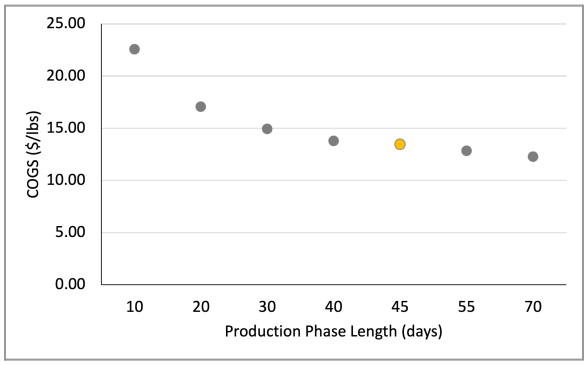

Figure 50: A Production Cycle Efficiency graph visualizing the facility's operational cycle, batch production rates, and overall output.

Summary

SuperMeat's journey toward cultivated meat production has been driven by a commitment to achieving cost efficiency without compromising product experience and nutritional quality. At the heart of this effort lies a robust production process that supports continuous differentiation into muscle and fat tissues.

A key breakthrough has been the successful implementation of a continuous production process, enabling a smooth transition from cell expansion to differentiation and ensuring a steady output of cultivated muscle and fat. By optimizing nutrient management and adopting a chemically defined medium, SuperMeat has eliminated the need for animal-derived components, establishing a more sustainable and reliable production model.

The company's ability to reach high cell densities within a short timeframe, coupled with rapid differentiation protocols, marks a significant breakthrough in cultivated meat production. These technical advancements offer a glimpse into a future where cultivated meat can be produced at scale, providing a sustainable alternative to conventional meat.