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Fostering European Cellular Agriculture for Sustainable Transition Solutions

Bioreactor specifications for industrial production of cultured meat/cultured seafood

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Executive Summary

Bioreactors must meet specific requirements for their application in the production of cultured meat and cultured seafood (CM/CSF). This report presents findings from a comprehensive literature and patent review of various bioreactor concepts and processes for CM/CSF production. It also suggests Key Performance Indicators (KPIs) for bioreactor design in CM production.

Additionally, we report results from an online survey conducted with companies that manufacture CM/CSF bioreactors in order to gather insights into their products and usage. Furthermore, we propose a concept for bioreactor parallelization across different production scales and discuss suitable manufacturing systems (centralized or decentralized) for each concept.

By developing appropriate concepts for bioreactor parallelization, the report addresses key challenges related to scaling up production and promotes sustainable practices in CM/CSF manufacturing.

Overview of the different bioreactor concepts and processes for cultured meat production

Introduction

Bioreactors play pivotal roles in CM/CSF production by providing the ideal conditions necessary for larger-scale cell expansion. In this task, we conducted a comprehensive literature and patent review to map the current and emerging bioreactor concepts relevant to CM/CSF production. We have recently published a manuscript titled **"Bioreactor parameters and systems for cultured meat production"** in the Future Foods journal (Ngwa et al., 2025) where we discussed the state of the art in bioreactor systems used for CM/CSF production, highlighting their characteristics and applications, advantages and disadvantages, the effect of key process parameters, stimuli for cell differentiation and larger-scale strategies for CM production. We also highlighted key performance indicators for the bioreactor design for CM production.

Major bioreactor systems for CM production

Bioreactors are designed to support the growth and differentiation of animal cells in a controlled environment. In this section, we provide a summary of the main types of bioreactor concepts (Figure 1) used for CM/CSF production and their specifications, including key aspects like advantages and disadvantages, potential mode of operation, potential cell cultivation format, maximum working volume, and approximate Technology Readiness Levels (TRLs). Please see the summary in Table 1.

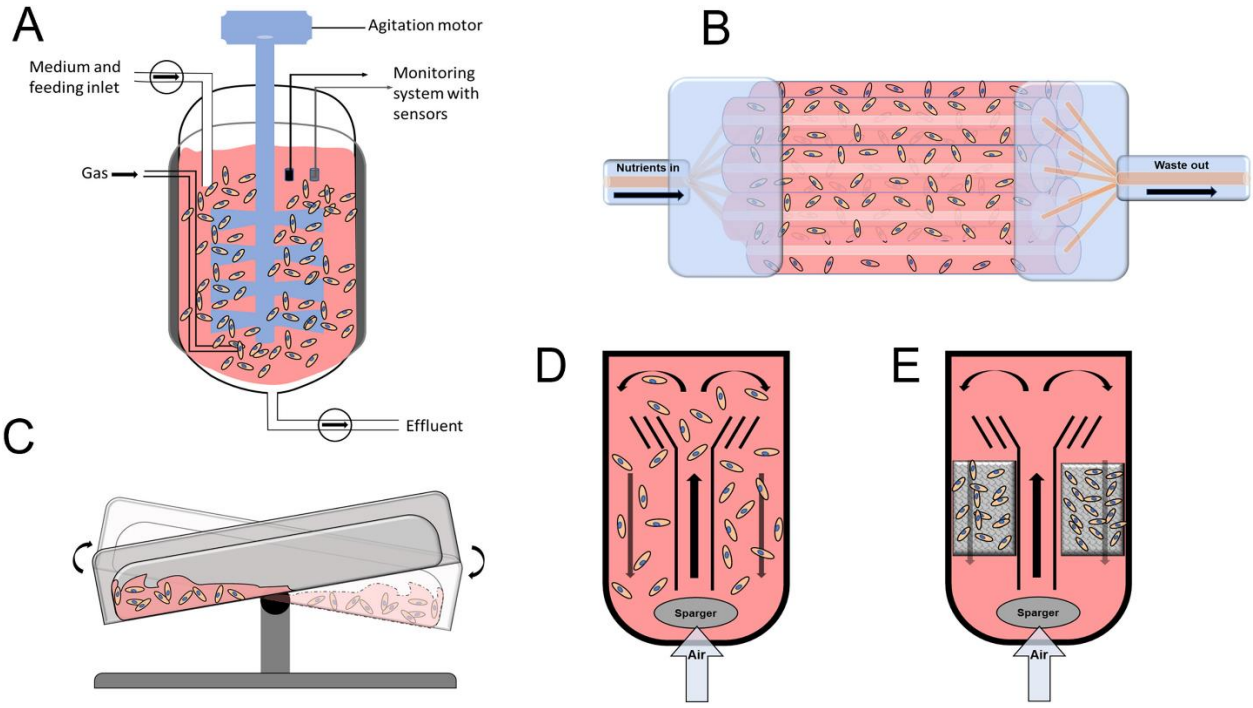

Figure 1. Main bioreactor systems for CM production (cells not drawn to scale). (A) Stirred-tank bioreactor (STR). (B) Hollow-fiber bioreactor (HFB). (C) Rocking-motion bioreactors (RMB). (D) Airlift bioreactor (ALB). (E) Fixed-bed bioreactor (FBB). Obtained from Ngwa et al., 2025

Table 1: Main bioreactor concepts for CM/CSF with specifications (adapted from Ngwa et al. (2025)). Batch (B), Fed-batch (FB), Perfusion (PF), Single cells (SC), aggregates (AGG), Scaffold (SF), Microcarriers (MC), Technology Readiness Levels (TRLs).

Bioreactor concept	**Pros**	**Cons**	**Potential mode of operation**	**Potential Method of cultivation**	**Max. working volume or area**	**Max. cell density (Cells/mL)**	**CM/CSF TRLs**	**References**
Stirred tank (STR)	• Highly characterized with a high degree of know-how • Simple design and highly adaptable • Enables easy scale-up • Can be used for cell expansion and differentiation	• Generates substantial shear stress • Detaching cells from microcarriers in bioreactor may pose problems for CM if microcarriers are not edible and suspension cell culture is not feasible	B/FB/PF	SC/AGG/MC	250,000 L (under construction)	Not specified	5–7	GoodMeat, 2022
Hollow fiber (HFR)	• Generates low shear stress suitable for CM production • Compact design that supports high cell densities in small volumes • Highly efficient diffusion process due to semipermeable membrane, enabling proper nutrient delivery to cells	• Material of fiber may pose problems with cell harvesting for CM production • System results in the formation of concentration gradients • May be difficult to monitor cell growth and other required in process control parameters	PF	SF	2.1 m^2	>1 x 10^8	4–5	Pan et al., 2023
Rocking motion (RMB)	• Allows efficient mixing with minimal shear stress • The use of disposable bags may simplify bioprocess workflow and reduce risk of contamination	• At very high volumes, the efficiency of mixing and gas exchange may decrease • Scale-up is challenging due to large installation space and size limitations for bags $\leq$ 1m^3 being 1-5% of other commercial reactor types. • Production cost increase due to requirement for single-use bags and the high number of batch analysis	B/FB	SC/AGG/MC	1000 L	1 x 10^7	4–5	Kim et al., 2024
Airlift (ALB)	• Low shear stress due to air-driven agitation • Efficient oxygen transfer and mixing at small scale • Operational cost may be lower than for STRs	• Mixing problems may arise when cell viscosity is high • Scale-up is challenging • Potential foam formation	B/FB/PF	SC/AGG	300 m^3	>2 x 10^8	4–5	Li et al., 2020
Fixed-bed (FBB)	• Low shear stress and easy medium exchange • Allows direct CM production on scaffold	• May pose problems during cell harvesting if scaffold is not edible • Scaling up challenging	FB/PF	SF	600 m^2	> 5 x 10^8	4–5	Goral et al., 2024

Novel innovative bioreactor concepts for CM/CSF

From the main bioreactor concepts shown in Figure 1 and Table 1, inspiration has been drawn to develop novel, fit-for-purpose bioreactors specifically designed for the production of CM/CSF (Figure 2). These patented bioreactor designs and technologies aim to optimize cell growth, differentiation, and tissue formation in a controlled manner.

While these novel bioreactor concepts utilize small bioreactors that operate with limited volumes, which may not initially seem suitable for larger-scale CM production, they can be adapted for larger-scale operations by scaling out, running multiple small bioreactors in parallel. Table 2 below provides a summary of various patented bioreactor concepts for CM production, highlighting their novelty/advantages, and limitations, as well as the cell cultivation methods and potential modes of operation.

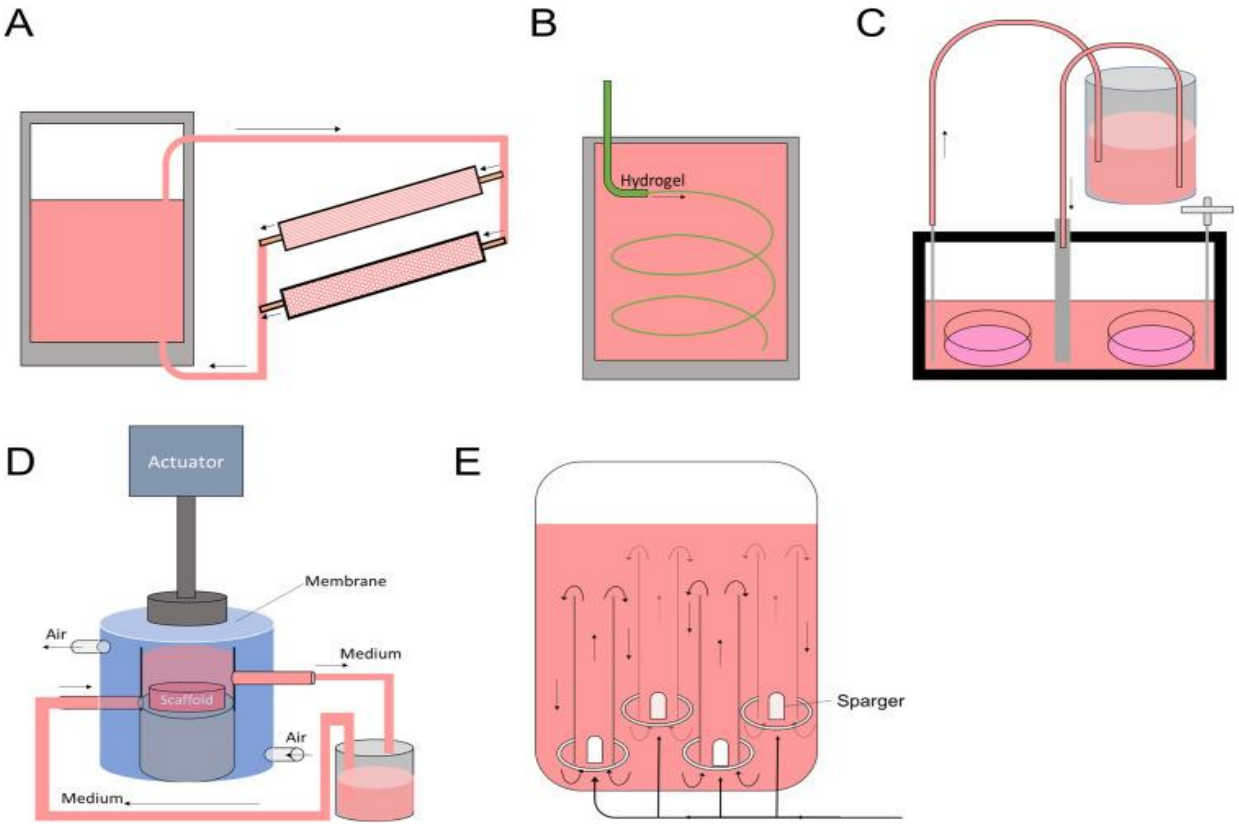

Figure 2: Novel bioreactor concepts for CM production. (A) Pipe-based bioreactor for producing CM (Upside Foods). The pipes bioreactor contains substrates which is rotatable to allow adherent cells to attach. (B) Bioreactor for cultured fat (Mosa Meat). A vessel with an injection of hydrogel precursor fluid to fabricate a fiber for fat cell cultivation. (C) Scaffold bioreactor with scaffold trays containing scaffolds and a circulatory system to provide medium to the cells on the scaffolds (ARK Biotech). (D) A bioreactor for cultivating cells with a mechanical stimulation system to promote the cell maturation in a scaffold (Fraunhofer IME). (E) Cluster ALB with many spargers driven vertical circulation system allowing for efficient mass transfer (ARK Biotech). Figure obtained from Ngwa et al., 2025

Table 2: Novel bioreactor concepts for CM production (Adapted from (Ngwa et al., 2025)). Batch(B), Fed-batch (FB), Perfusion (PF), Single cells (SC), aggregates (AGG), Scaffold (SF), Technology Readiness Levels (TRLs)

Patent number and holder	**Bioreactor type**	**Novelty /advantage**	**Limitation**	**Cultivation method**	**Mode of operation**	**TRLs**	**Reference**
WO2024085898-A1 Upside Food	HFB	Pipe-based bioreactor contains substrate for cell attachment and it is rotatory to allow mixing of medium for cell cultivation	Narrow pipe geometries with high density cell growth may increase the difficulty to maintain sterile and clog-free condition	SF	B/FB	3–4	Benton & Müller-Auffermann, 2024
WO23224484-A1 Mosa Meat	STR	Able to fabricate cell-embedded hydrogel fiber in container vessel for fat cell cultivation	Precise control is required to fabricate hydrogels, and scaling-up is complicated	SF	B/FB	3–4	Mazari et al., 2023
WO2023211726-A1 ARK Biotech	FBB	Scalable layered scaffold-tray architecture to hold the scaffold with pulsatile flow over cells for enhanced transport	Intermittent perfusion can lead to uneven nutrient distribution across layers	SF	B/FB	3–4	Zheng et al., 2023a
WO2021148663-A1 Fraunhofer-Gesellschaft	FBB	Bioreactor is able to provide a mechanical stimulation to promote cell maturation in scaffold or hydrogel	Require compressible scaffold/hydrogel to be stimulated over the batch runs	SF	B/FB	3–4	Vogel & Schillberg, 2021
WO23211696-A1 ARK Biotech	ALB	Sparger driven air lift vertical circulation system allowing for efficient mass transfer	Require precise real-time monitoring and control to spargers and loop	SC/AGG	PF	3–4	Zheng et al., 2023b

Critical process parameters for CM/CSF production

To mimic the physiological conditions of living tissues and produce muscle and fat cells similar to those in conventional meat, it is essential to identify, monitor, and control critical process parameters that may directly impact the quality or safety of the final product. In the table below, we summarize the role of some critical parameters for CM/CSF production, their impact due to deviation, and control measures (Table 3).

Table 3: Critical parameters for CM/CSF

Critical parameter	**Role**	**Standard value**	**Impacts of deviation**	**Control method**
pH	Influences cell metabolism and nutrient uptake	7.2–7.4	A change in pH may disrupt protein structure and cause a loss of function, which affects cellular processes such as respiration, nutrient uptake and metabolism, proliferation and differentiation	Adding CO_2 to lower pH or addition of sodium bicarbonate to raise pH
Oxygen	Necessary for aerobic processes, cellular respiration and metabolism	*In vivo* typically approx. 1 - 7%, in cell cultures (correcting for CO2 and vapor related displacement) approx 18%, from normal atmospheric 21%	Low O_2 can causes hypoxia and lactate buildup; high O_2 can generate reactive oxygen species	Adjusting gas flow rate, bubble size, and mixing speed
Carbon dioxide	Regulates pH and cellular metabolism	Maintained at 5–10%	Excessive CO_2 lowers pH and can affect enzyme activity and metabolism	Balance CO_2 concentration
Temperature	Regulates biochemical and physiological processes	37 °C (CM) and 15–30 °C (CSF)	Deviations can lead to stress responses, protein misfolding, altered metabolism, and lower viability	Temperature sensors and jacketed heating/cooling systems
Cell density	Determines scalability and productivity	Depends on mode of operation and bioreactor type	Over growth leads to nutrient limitation and waste accumulation	Capacitance or optical sensors
Agitation and Shear stress	Ensures homogeneous mixing and oxygen transfer	Depends on bioreactor type	High shear stress damages cells Can results in foaming	Exploit low shear impellers, microcarriers, or bioreactors system with limited shear stress
Cell differentiation	Drives muscle and fat cell formation	Can require a mix of growth factors, mechanical, chemical and/or electrical stimuli	Incomplete differentiation results in meat with poor quality and texture	Controlled stimulation cues
Scale-Up Considerations	Enable production of large-scale CM/CSF	Volumes up to 20,000L per bioreactor	May result in shear stress, poor gas and nutrient transfer	Computation fluid dynamics modeling and scaling -out by parallelization
Sterility	Confirms aseptic process		Batch loss, toxins, slow growth, safety risks	Monitor and control sterility e.g. through PCR screening for contamination
Cell quality	Determines the health of cultures, identity of cells, genetic stability and product functionality		Low yield, impurities, growth and texture drift, safety risks	Regularly check cells for impurities, lineage/species and genetic stability

Key performance indicators (KPIs) for the design of bioreactors for CM production

From the literature review, we set KPIs for bioreactor design and process optimization for CM/CSF production summarized in Table 4. We recommend that these KPIs should be considered when designing bioreactors or optimizing processes for the production of CM/CSF. The KPIs are also of particular importance in an industrial context when developing strategies for scaling-up production.

Table 4: Key performance indicators (KPIs) for the design of bioreactors for CM and CSF production (adapted from Ngwa et al. (2025))

KPI	Description
Bioreactor type	The choice of bioreactor design influences the mass transfer, mixing and shear stress. It also determines the operating volume and scale-up potential. Therefore, the bioreactor type must be considered for CM production and scale-up.
Mode of operation	For larger-scale CM production, the fed-batch or continuous supply of media to the cells is preferred for efficient cell proliferation.
Fluid dynamics and agitation systems	Essential to limit shear stress, and to control the temperature and gas gradient.
Proliferation/ differentiation	The bioreactor should support a high cell density, thus ensuring robust cell proliferation and differentiation as well as potentially steps of final product formulation (e.g. addition of non-dissolvable fibers, preservatives measures). Moreover, the cultivation process should be conducted in a manner that maintains cell viability and minimizes cell death.
Ease of operation	The ease of operation ensures that the processes of feeding, extraction, and control are straightforward and efficient. This allows for the smooth handling of the system and minimal downtime while maintaining precise control over the bioprocess.
High yield and reproducibility of results	Achieving high yield and reproducibility is critical to ensure that the system consistently supports optimal cell growth and production efficiency over multiple cycles while maintaining product quality.
Ease and cost of maintenance	The bioreactor should be designed to have minimal maintenance requirements and to be cost-effective. That means minimal downtime and a design compatible with easy access to its components. This guarantees that routine maintenance and repairs can be carried out with minimal operational disruption and reduced long-term maintenance costs
Durability	The bioreactor should be able to withstand continuous use over fixed periods, maintaining structural integrity and performance under various operating conditions, including pressure/temperature fluctuations, and chemical exposure.
Operating volume and upscaling	The bioreactor should be designed in such a way that it can be readily scaled up without altering cell growth.
Cleaning and sterilization	Cleaning and sterilization of the bioreactor should be easy, inexpensive and compliant with the regulations.
Sterility risks	A sterile environment is essential to prevent contamination from unwanted microorganisms, which can compromise the entire CM production process.
Process monitors and controls	Effective process monitoring and control are essential, allowing for real-time adjustments to parameters such as temperature, pH, oxygen levels, and nutrient supply to maintain optimal conditions and ensure consistent product quality throughout the bioprocess. Failure rate and batch to batch variation also should be effectively monitored.
Sustainability	The bioreactor design and process should minimize the consumption of media, energy, and water during the process.
Material properties and equipment selection	Appropriate materials and equipment ensure optimal performance, durability, and compatibility of the bioreactor with the bioprocess. The materials must demonstrate chemical resistance and mechanical strength. The equipment must be chosen to enhance process control, scalability, and efficiency, in alignment with the specific demands of the cell culture environment.

Survey on bioreactors for CM/CSF

To further gather information on bioreactor specifications and their processes currently used for CM/CSF production, we conducted an online survey from March to August 2024 by reaching out to companies that manufacture bioreactors potentially suitable for this purpose.

Survey questions and results

A total of 38 different companies were contacted to participate in the online survey, which aimed to gather answers to questions related to various aspects of bioreactor design and CM/CSF process development. Out of the 38 companies contacted, 10 responses were provided. Upon analyzing the results, we discovered that the same company had submitted three responses from different individuals. Consequently, we decided to exclude two of these responses, resulting in a final analysis based on 8 unique responses (Figure 3).

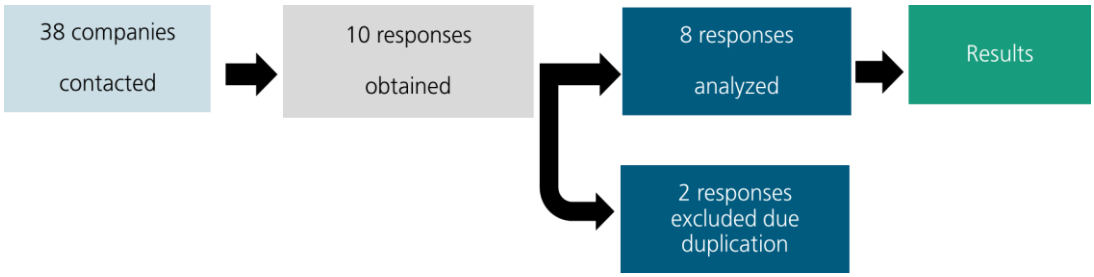

Figure 3: Response rate to online survey on bioreactors for CM/CSF

What type of bioreactors that your company produces are (or could be) used for CM/CSF?

To determine the type of bioreactor that the companies produce that can be used for CM/CSF production we asked them the above question. The results indicate that the companies produce multiple types of bioreactors that they consider suitable for CM/CSF production. However, stirred tank bioreactors were the most favored, with 5 out of 8 companies reporting their production for CM/CSF applications (Figure 4). This was followed by perfusion bioreactors, cited by three companies, and 2D rocking motion bioreactors, mentioned by two companies (Figure 4).

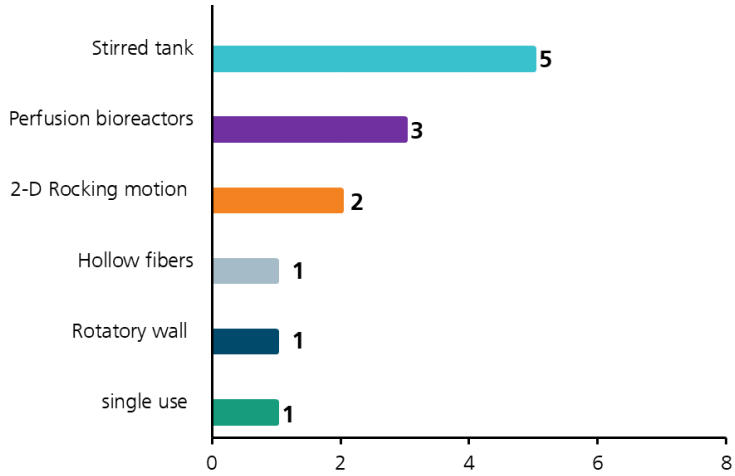

Figure 4: Bioreactors produced for CM/CSF production

What is the maximum working volume and maximum achievable cell density in your bioreactor?
Most of the companies indicated that the maximum working volume ranges from <1,000 L to 50,000 L, accounting for 87.5% of the responses (Figure 5A). Concerning the maximum cell density achievable, 50% of the companies believe that a density of 10^6 to 10^7 cells/mL can be attained, while the other half estimates that densities <10^7 cells/mL are achievable (Figure 5B).

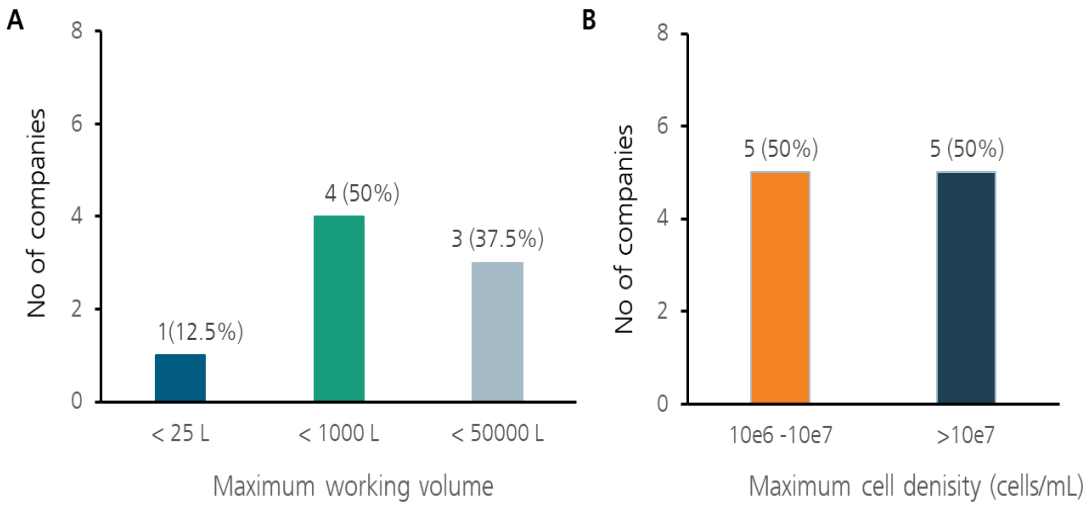

Figure 5: Maximum working volume and cell density in the bioreactor. (A) Maximum working volume in bioreactors. (B) Maximum cell density in bioreactors

For which of the following can the bioreactors be used?
We also inquired whether the bioreactors could be utilized for cell expansion, differentiation, or both. Six companies (75%) indicated that the bioreactors are suitable for both cell expansion and differentiation, while 25% stated that the bioreactors can be used for cell expansion only (Figure 6).

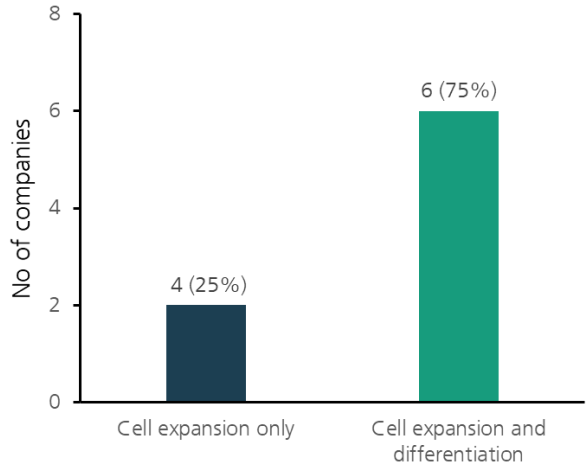

Figure 6: Purpose of bioreactor use for CM/CSF presentation

Cells from which sources (e.g., animal species) have (to your knowledge) already been cultivated in the Bioreactors?

To gain insight into the cell sources cultivated in the bioreactors produced by the companies, we asked them which cell sources, to the best of their knowledge, have been cultured in their bioreactors. Fifty percent of the companies mentioned multiple cell sources, 25% identified a single cell source, and 25% did not provide any response (Figure 7A). The most frequently cited species for cell sourcing were bovine and poultry, with 4 out of 8 companies indicating that these sources can be cultivated in their bioreactors (Figure 7B).

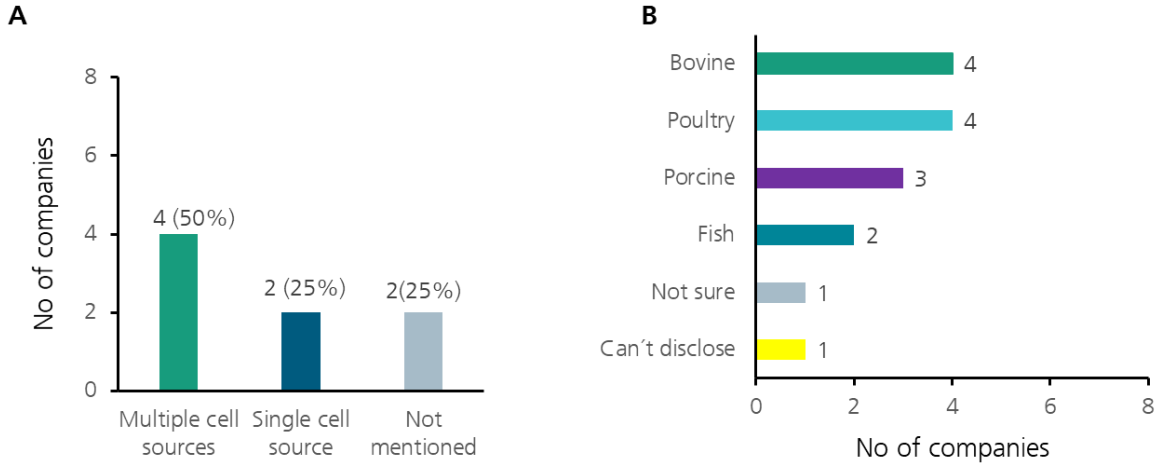

Figure 7: Cell sources cultivated in bioreactor. (A) Cell sources cultured in bioreactor. (B) Name of animal source

Which cell types have (to your knowledge) already been cultivated in the bioreactors and how are they cultivated?

To determine the main cell types used for CM/CSF production, as well as the methods of cell culture (suspension or scaffolds), we asked the companies which cell types have been cultivated in their bioreactors and how they are cultured. Five out of 8 companies reported cultivating mesenchymal stem cells, followed by induced pluripotent stem cells (4 companies) and embryonic stem cells (3 companies) (Figure 8A). Regarding the method of cultivation, 50% of the companies indicated that they use suspension cultivation for single cells or aggregates, while the remaining half mentioned suspension cultivation on scaffolds such as microcarriers (Figure 8B).

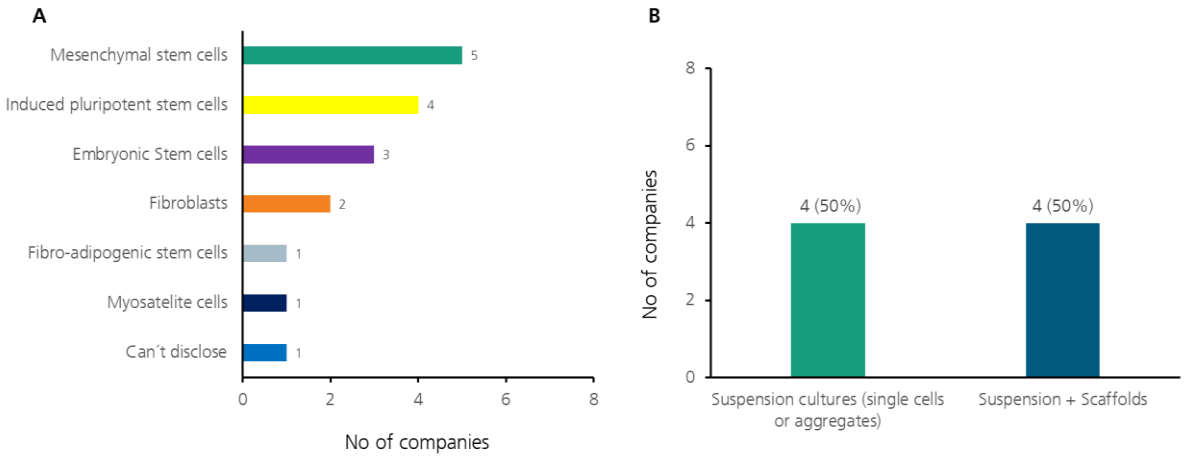

Figure 8: Main cell types (A) and method of cell culture (B) in bioreactors

In what way can the cells be stimulated within the bioreactors to promote differentiation?

To explore the methods used to stimulate cells in the bioreactors for enhanced cell differentiation, we posed the relevant question to the companies. Four out of 8 companies indicated that they employ mechanical and chemical stimulation, while 2 companies mentioned a combination of chemical, mechanical, and electrical stimulation. One company reported using chemical stimulation only, and one company was uncertain (Figure 9).

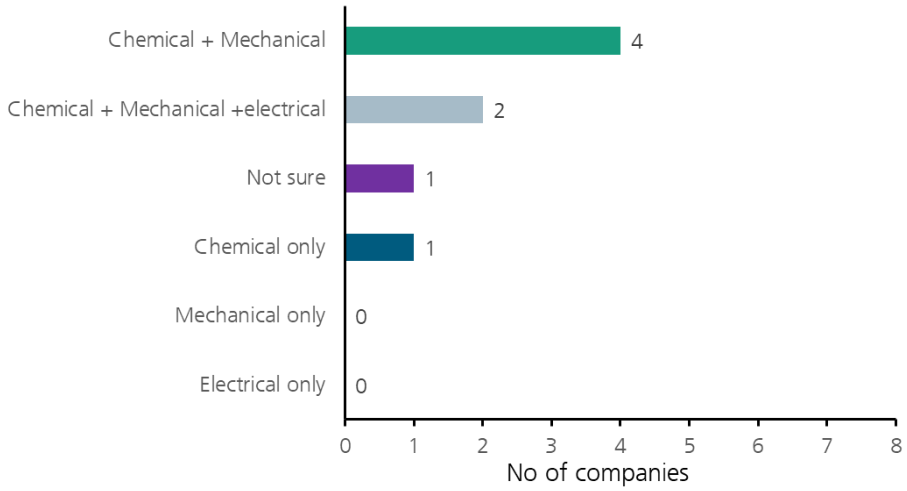

Figure 9: Ways to stimulate cell differentiation in bioreactors

On which feeding/extraction mechanisms are your bioreactors operated on?

To determine the modes of operation of the bioreactors produced by the companies, we asked them the relevant question. Interestingly, 62.5% of the companies indicated that they utilize all three modes of operation (batch, fed-batch, and continuous), while the remaining 37.5% indicated that they use both fed-batch and continuous modes (Figure 10).

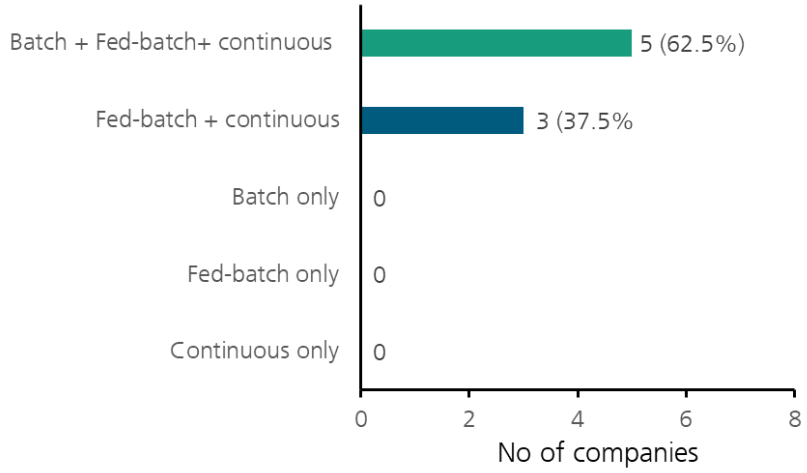

Figure 10: Mode of bioreactor operation

How can critical parameters be monitored in your bioreactors?

We sought to investigate how critical parameters, such as pH, oxygen, CO_2, shear stress, temperature, cell density, glucose, glutamine, lactate, ammonia, and cell differentiation, can be monitored in bioreactors produced by the companies. The results indicate that basic parameters, such as pH, oxygen, CO_2, and temperature, can be measured either online or in-line, while

parameters like cell density, glucose, glutamine, lactate, ammonia, and cell differentiation are primarily monitored offline or at-line (Figure 11). In-line monitoring allows for monitoring directly inside the bioreactor, on-line analyzers measure automatically through a connected sampling loop, at-line tests use manually taken samples analyzed near the bioreactor, and off-line measurements analyze samples in external labs. Each monitoring method differs in automation, response time, and impact on real-time process control.

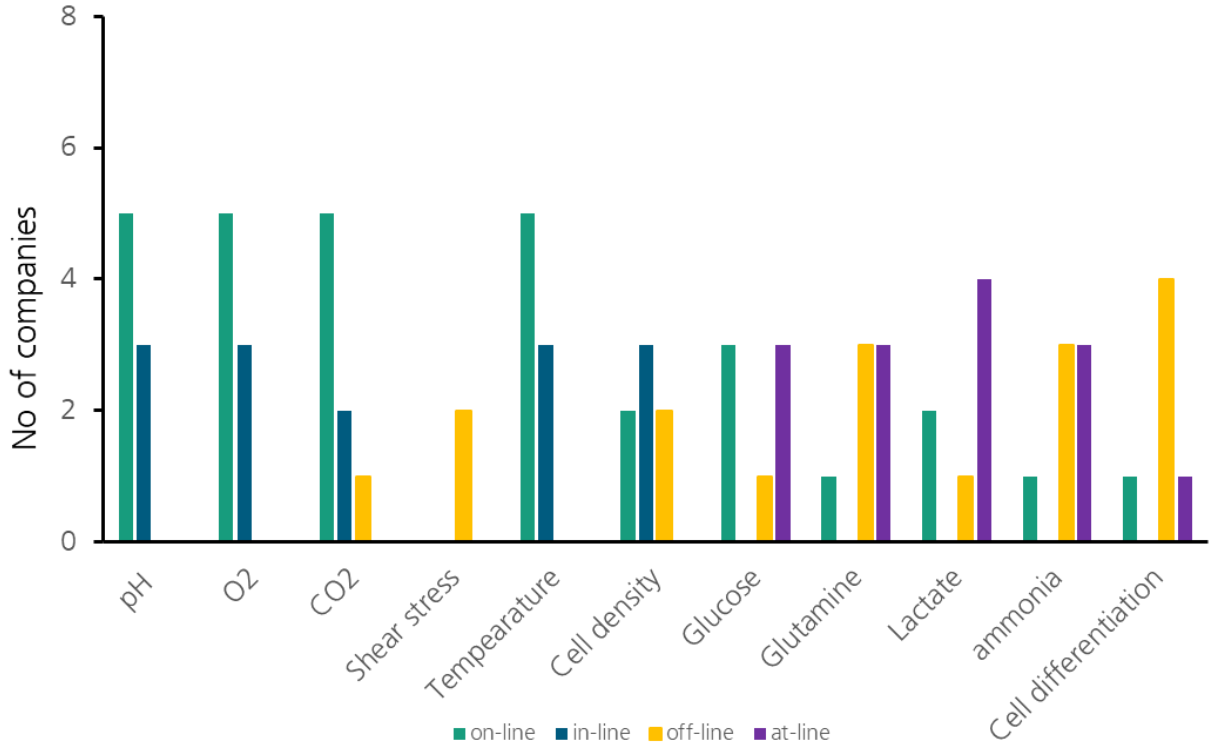

Figure 11: Methods of monitoring of critical parameters in bioreactor

What are feasible strategies for further scale-up of the bioreactors?

Inquiring about the feasibility of further scale-up of the bioreactors, 75% of the companies indicated that the most feasible strategy involves scaling up by increasing the size of the bioreactor in conjunction with scaling out (parallelization). The remaining 25% suggested that scale-up could be achieved solely through size increase (Figure 12).

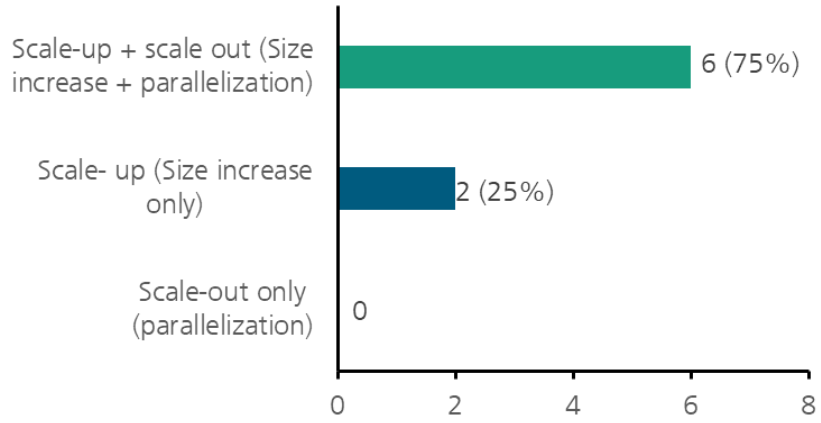

Figure 12: Feasible strategy for large scale production

Which sterilization methods are compatible with your bioreactors?

We also asked the companies which sterilization methods are compatible with the bioreactors they produce. The majority of the companies (62.5%) mentioned multiple sterilization methods (Figure 13A) with thermal treatment (autoclaving) plus irradiation being the most used (37.5%, Figure 13B).

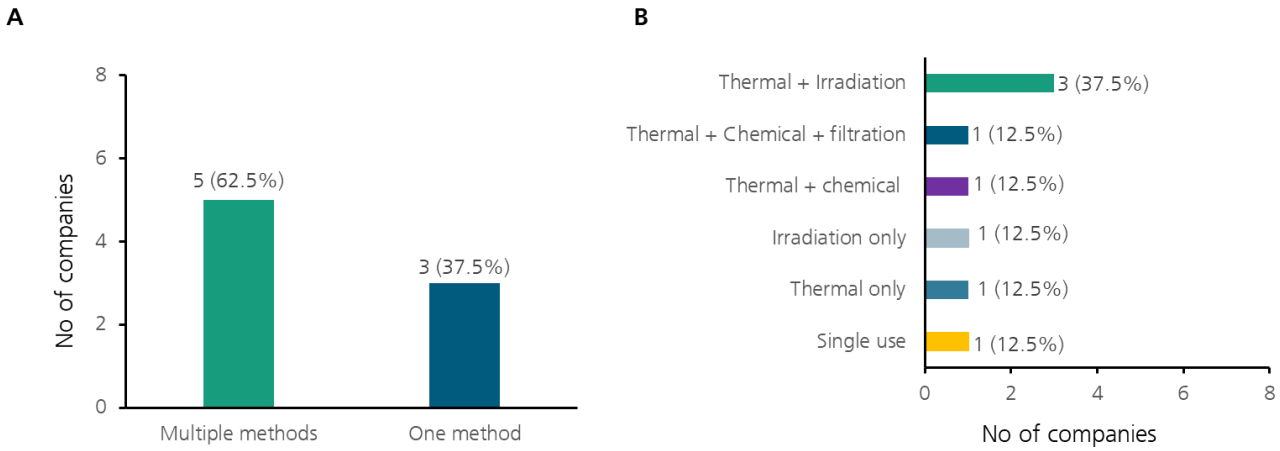

Figure 13: Methods for bioreactor sterilization. (A) Number of methods used. (B) Types of methods used

Can the bioreactor be modified/upgraded over time (for example by implementing additional modules such as sensors, mixing elements, feeding or extraction modules)?

The ability to modify or upgrade a bioreactor over time is advantageous, as it allows for adaptation to additional features suitable for the process. To gather information on this, we asked whether the bioreactors they produce can be modified or adapted. 87.5% percent of the companies affirmed that their bioreactors can be modified or upgraded, while 12.5% indicated that they cannot (Figure 14).

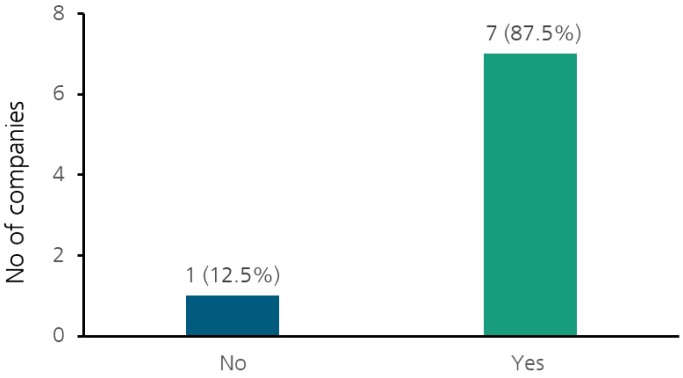

Figure 14: Can the bioreactors be modified or upgraded?

Which type of materials do the biological samples (cells, liquids, scaffolds, etc.) come into contact with inside the bioreactors?

We also aimed to identify which materials come into contact with biological samples during the cultivation process in the bioreactors. The companies mentioned that multiple materials come in contact with the bioreactors. Stainless steel, plastic, and glass were reported as the primary materials that interact with the biological samples (Figure 15).

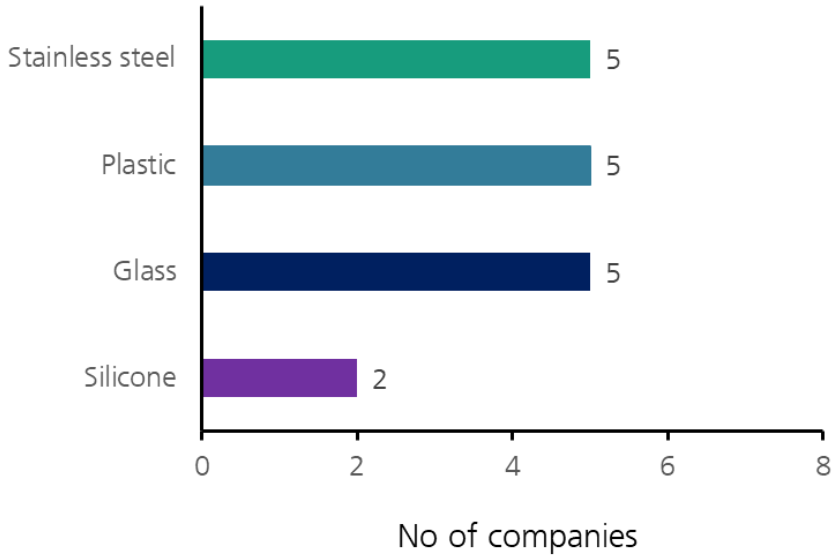

Figure 15: Materials biological samples come in contact with in a bioreactor

Summary and highlights from survey

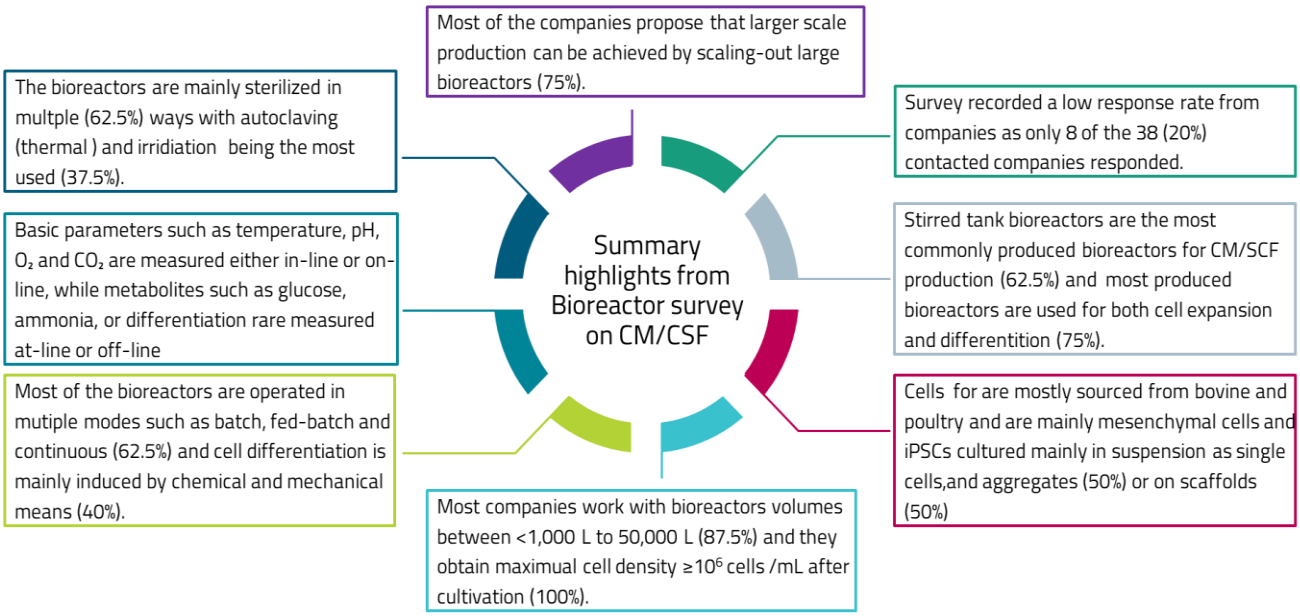

Figure 16: Summary of survey highlights

Conceptual framework for bioreactor parallelization for industrial CM/CSF production

Introduction

CM/CSF represents an innovative technology for meat production, and commercialization can only be achieved through the larger-scale production in bioreactors. Despite the high promise of this technology, commercialization remains constrained by key challenges, including securing regulatory approval, limited product performance, high production costs, and insufficiently optimized larger-scale production strategies. One of the most critical challenge is the development of scalable and efficient bioprocessing systems that can hasten regulatory approval, support industrial-level production and commercialization while maintaining product quality, sustainability and economic feasibility.

In this section, we present a conceptual framework for bioreactor parallelization as a core strategy to increase the production capacity of CM production in a sustainable manner. We propose four different parallelization scales (small, medium, large, super large) and propose their integration into either centralized or decentralized production models, aiming to enhance throughput, improve process control, or reduce investment costs. The concept contributes to the foundational knowledge required for the development of next-generation cultured meat biomanufacturing systems. These insights have the potential to accelerate the transition of CM from laboratory-scale innovation to a commercially viable sustainable food production.

Bioreactor parallelization

As opposed to bioreactor scaling-up which entails simple increasing the size of one large vessel, bioreactor scaling-out or parallelization involves using multiple small bioreactors in parallel. Although successful scaling-up production using a single large bioreactor can better deal with production demand, conditions that are optimized in small-scale bioreactors do not really translate at a very large scale. Several issues with critical parameters, including mixing inefficiencies, oxygen, CO_2, and nutrient gradients, often arise in very large-scale bioreactors (Ballani et al., 2020; Chen et al., 2022), which can result in high cell death, poor cell differentiation, and low yields. Apart from the above problems, using a single larger-scale bioreactor for CM production is a risky endeavor since contaminations, equipment failures, and process deviation can lead to the loss of an entire batch, resulting in great financial losses and disruption of the supply chain (Ngwa et al., 2025). Other hurdles include the fact that large-scale bioreactors require more aggressive mixing, which introduces high shear stress to the animal cells, as these cells are highly shear-sensitive and fragile (Chen et al., 2022). Due to these challenges, researchers have suggested that decentralized strategies exploiting scale-out should be employed, which distributes production across geographic regions rather than attempting to concentrate in large central factories (Fish et al., 2022).

This approach reduces the complexity associated with scaling-up a single large bioreactor by maintaining the well-understood, optimized conditions of smaller bioreactors. Scale-out strategy also enables incremental scaling of production by adding more bioreactors to meet consumers

demand without the need for large capital investment (Fish et al., 2022). This strategy is also easier to adapt for example easy sterilization, has a reduced risk since if one bioreactor fails or is contaminated, the other can still continue to operate. It can also enable different bioreactors to be used for different purposes such as one for the seed train, cell expansion and for cell differentiation making the system highly flexible. Noteworthy, most of the companies who took part in the survey reported above recommended scaling-out as a feasible strategy for large scale CM production.

Below we propose four different parallelization scales (small, medium, large, super large) for integration in either centralized or decentralized production models, aiming to enhance throughput, improve process control and in some cases reduce investment costs. We also propose the fed-batch mode of operation of the bioreactors in the different parallelization scales as this reduces media cost and allows for manageable process control as compared to the continuous mode of operation.

Small scale parallelization (multiple bioreactors <10 L) – decentralized production for local markets

This proposed parallelization strategy involves the use of multiple bioreactors, each with a volume not exceeding 10 liters, to produce CM suitable for sale in local supermarkets or restaurants across Europe. It also favors production of CM at R&D and bench scale for process evaluation and product regulatory approval. This approach may leverage custom-made, user-friendly, and low-cost small bioreactors (TRL-3-6) to facilitate the production of CM near the point of research or sale (Figure 17).

A notable example of such bioreactor is the patented bioreactor (Vogel & Schillberg, 2021) , which incorporates an edible plant-based spongy scaffold placed in a 250 mL vessel (Figure 17). The plant-based scaffold production process was performed as a side project in Task 3.3 by the Fraunhofer IME and the results have been published in the Future Foods journal (Chiu et al., 2025). In the bioreactor setup, cells can be expanded through a seeding train and seeded onto the edible scaffold and differentiated through mechanical stimulation using a piston mechanism that mimics natural muscle contractions while also mixing the medium. Larger-scale production can be efficiently achieved by parallelizing multiple vessels (Figure 17).

Small-scale parallelization offers several key benefits, including a short seed train before the cells are utilized in the parallelization step. Depending on the type of bioreactor, the downstream process can be minimized. This is particularly beneficial when using plant-derived edible scaffold structures, as in the case of Fraunhofer IME bioreactor design. This strategy may also create ideal conditions for producing structured products, such as steaks. Additionally, if the system is properly designed, it can reduce resource consumption, such as media usage. The system can also be easily automated, facilitating media cycling and enhancing operational efficiency.

Most importantly, since CM has not yet been approved in Europe, this strategy could accelerate process development and due to its lower capital investment compared to larger systems, it may be leveraged by startups or research institutions to demonstrate industrial cultured meat production and expedite regulatory approval.

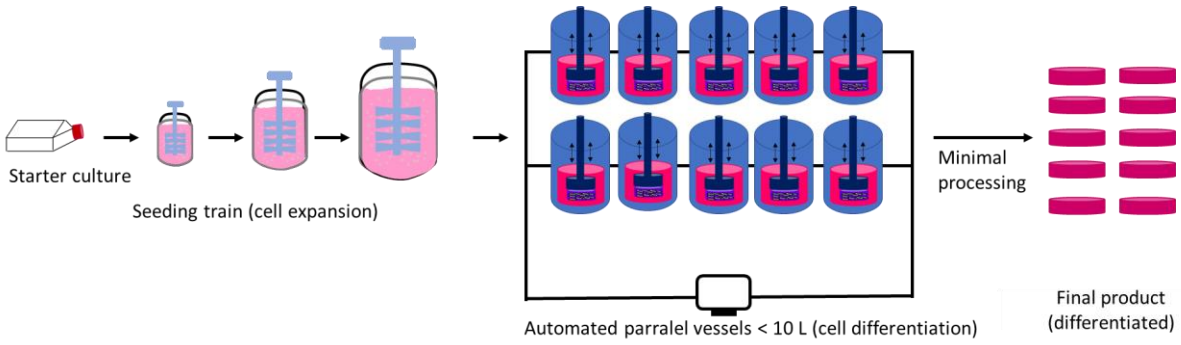

Figure 17: Schematic demonstrating concept for small-scale parallelization for CM production (diagram not drawn to scale)

The small-scale parallelization particularly supports decentralized production model for CM production with such strategy distributed all over Europe where most of the feedstock and labor can be obtained locally and the CM products sold close to the customers (Figure 18). Such strategy may also make use of renewable energy sources such as solar or wind to be able to run the facilities and improve sustainability of the process.

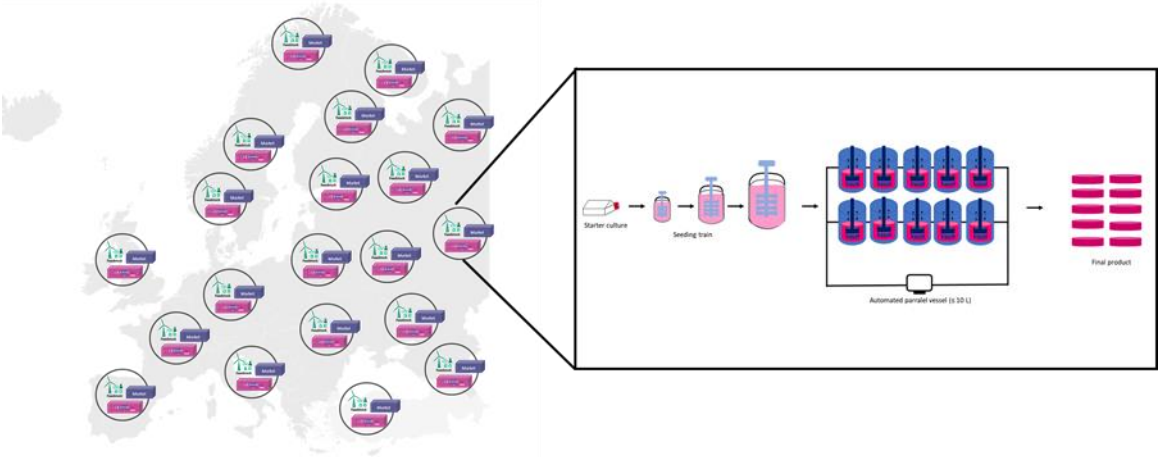

Figure 18: Decentralized small-scale parallelized CM facilities for local markets in Europe

Medium scale parallelization (multiple 100–2,500 L bioreactors) – decentralized on farms and villages

This parallelization strategy utilizes multiple bioreactors with volumes ranging from 100 to 2,500 liters, which is ideal for producing medium batches of CM products for regional European markets (Figure 19). It allows for the integration of other bioreactor systems, such as hollow-fiber bioreactors, rocking motion bioreactors, airlift bioreactors, or fixed-bed bioreactors, and small stir tanks, as they cannot accommodate large cell volumes (TRL 3-5).

The strategy may also necessitate a medium seed train for cell expansion, depending on the type of bioreactor employed and the process used. Downstream processing may be essential for differentiating and maturing the meat product if necessary. Medium-scale parallelization offers several advantages, including the ability to use different bioreactor systems, enabling tailored production approaches. In this strategy, upstream and downstream processes can be easily adjusted to meet specific needs such as including cell proliferation and differentiation, or not. The setup can be automated, enhancing control over process parameters. Medium batch sizes reduce the impact of process failures or unexpected outcomes and medium-sized bioreactors consume fewer

resources and simplify cleaning and maintenance. Overall, this strategy not only supports efficient production but also aligns well with the demands of regional markets.

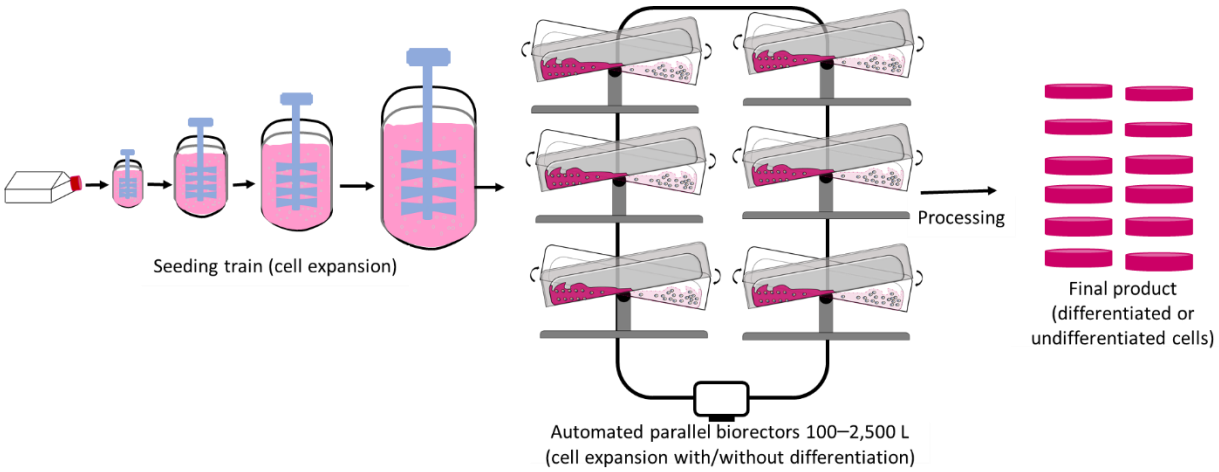

Figure 19: Schematic demonstrating concept for medium-scale parallelization for CM production (diagram not drawn to scale)

Medium-scale parallelization also favors decentralized production of cultured meat, where the production facilities could be developed at the regional level in animal farms where exploitation of resources for the meat production is used (cells, feedstock) and the final product is sold in this particular region (Figure 20).

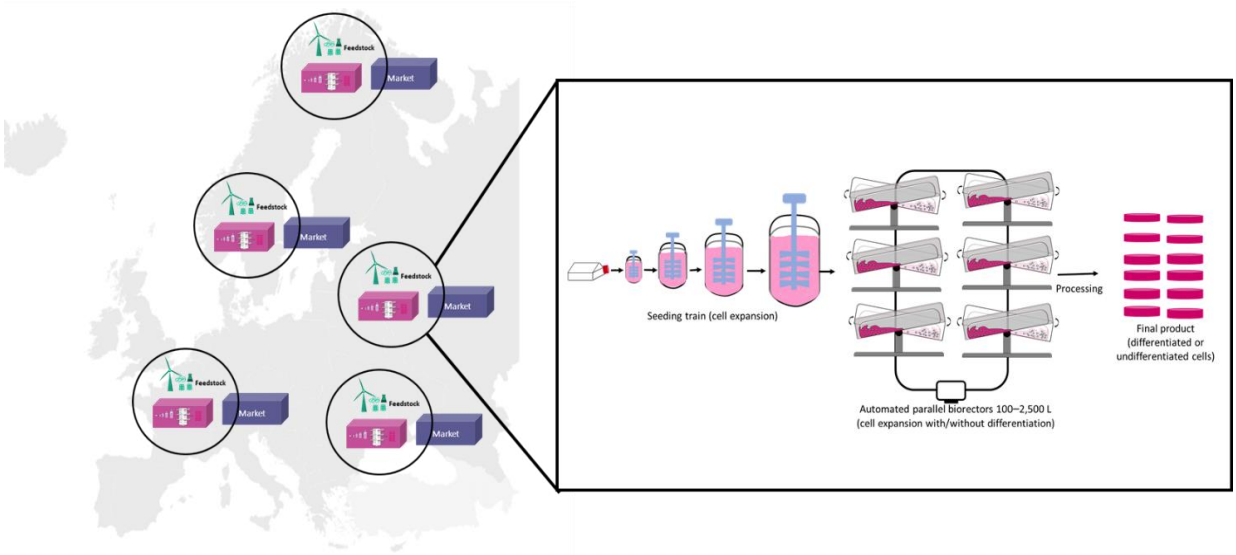

Figure 20: Decentralized medium-scale parallelized CM facilities for regional markets in Europe

Larger-scale parallelization (multiple 2,500–20,000 L bioreactors) – realistic centralization

This strategy utilizes multiple larger-volume (>2,500 - 20,000 L) stirred-tank bioreactors (TRL-3-4) to produce substantial batches of CM/CSF for global markets (Figure 21). While companies like GOOD Meat have announced plans for 250,000 L bioreactors, we believe that this approach may face significant challenges in industrial CM production unless the scale-up strategy using the bioreactors has been thoroughly been optimized and demonstrated. At the moment, we believe instead of relying on a single large 250,000 L bioreactor, the parallel operation of multiple large bioreactors, each with a capacity not > 20,000 L, can yield CM of superior quality and efficiency. Super-large

bioreactors have been optimized for CHO cell lines or other biopharma applications but have not been optimized for maximum CM productivity, which can compromise the consistency and uniformity of the final product, ultimately failing to meet consumer expectations and industry standards. By employing an optimal configuration of multiple well-studied STBs (>2,500 - 20,000 L), this strategy can mitigate the risks associated with contamination and facilitate easier sterilization processes. Ultimately, this approach is poised to deliver high-quality cultured meat to meet the partial demands of global markets.

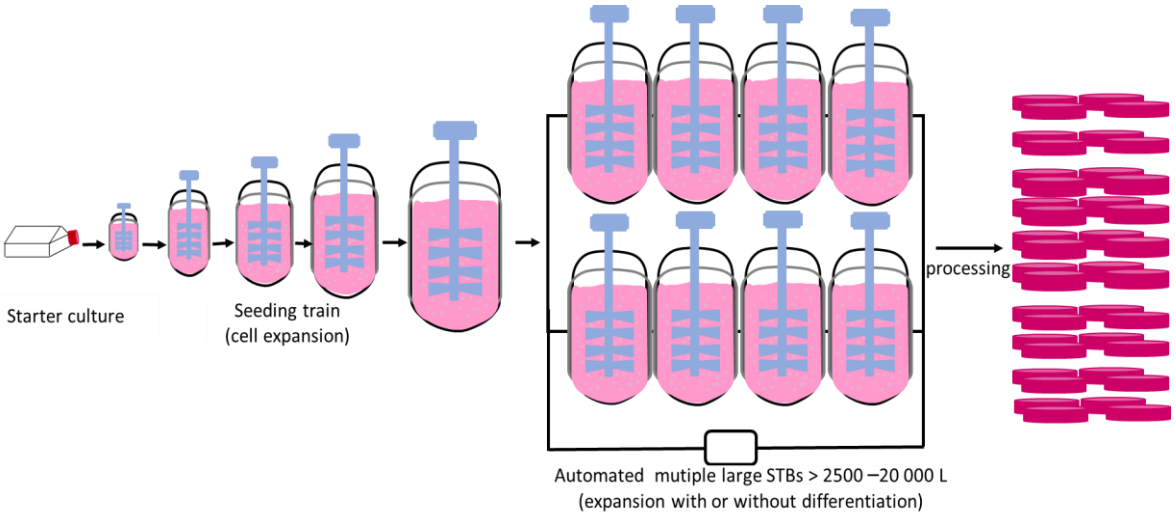

Figure 21: Concept for large-scale parallelization of CM production for regional markets

Larger-scale parallelization will promote a centralized production model, where the majority of feedstock is imported, and the products are transported and sold in the global market, particularly in Europe (Figure 22).

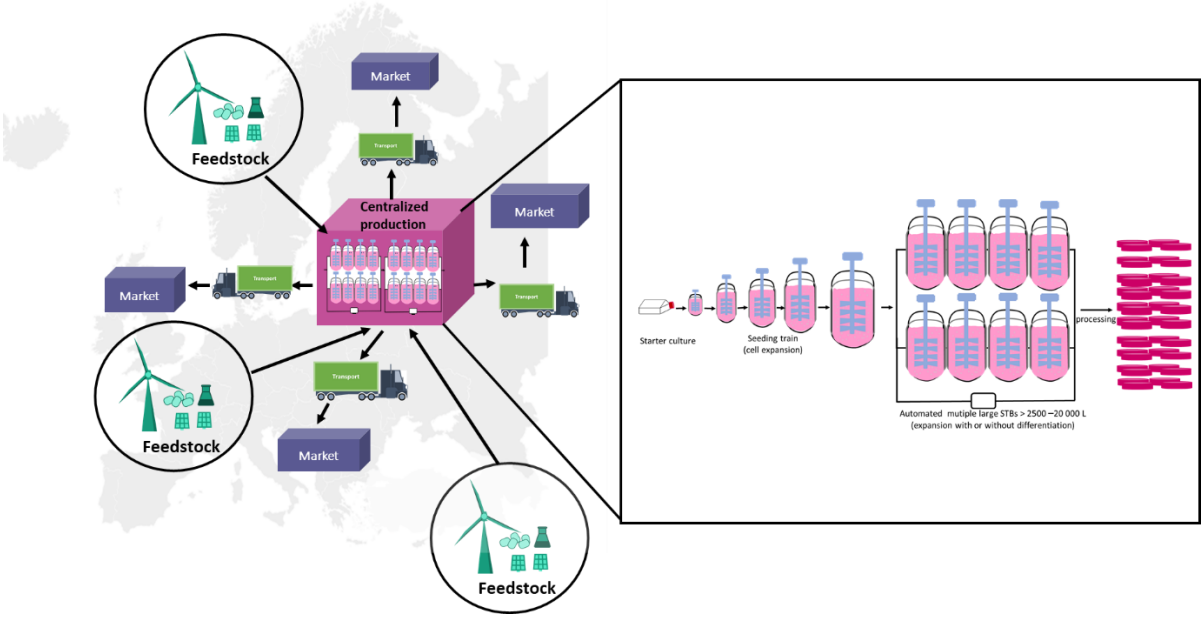

Figure 22: Centralized production of CM in larger-scale parallelization for the global market

Super large-scale parallelization (multiple bioreactors >20,000 L) – ambitious industrialization

This strategy is an ambitious long-term goal to exploit multiple bioreactors of > 20,000 L (TRL 2-3) for industrial CM production (Figure 23). With the rapid advancement of technology, strategies, and artificial intelligence, bioreactors will be developed in due time, allowing for the optimal cultivation of cells at extremely high volumes of > 20,000 L without affecting productivity, and with products expected to meet consumer demand.

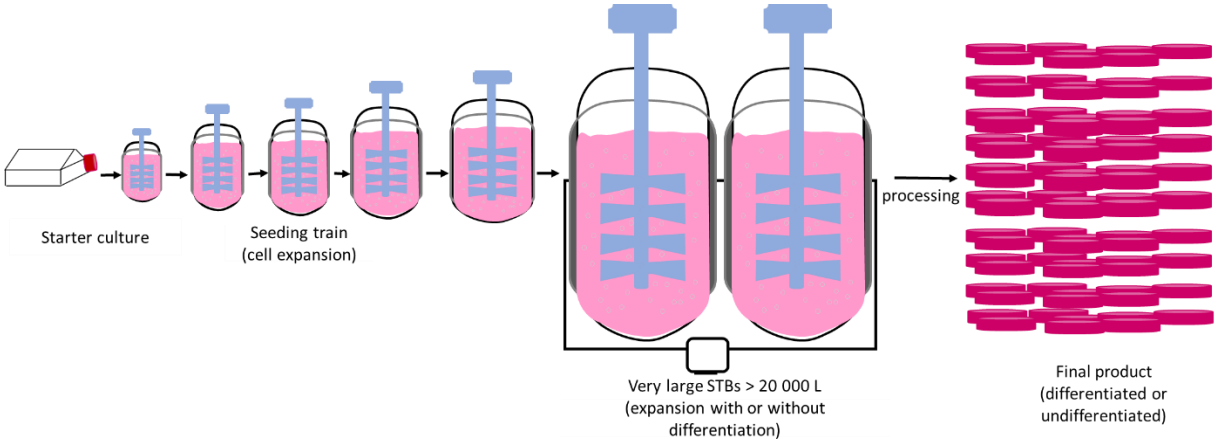

Figure 23: Concept for super large-scale parallelization of CM production (>20,000 L)

This approach will be a game changer in the field as it will provide a reasonable amount of CM to compete with traditional meat at the global market supporting a strongly centralized model of CM/CSF production where most of the feedstock will be imported and products distributed globally in Europe and outside Europe (Figure 24).

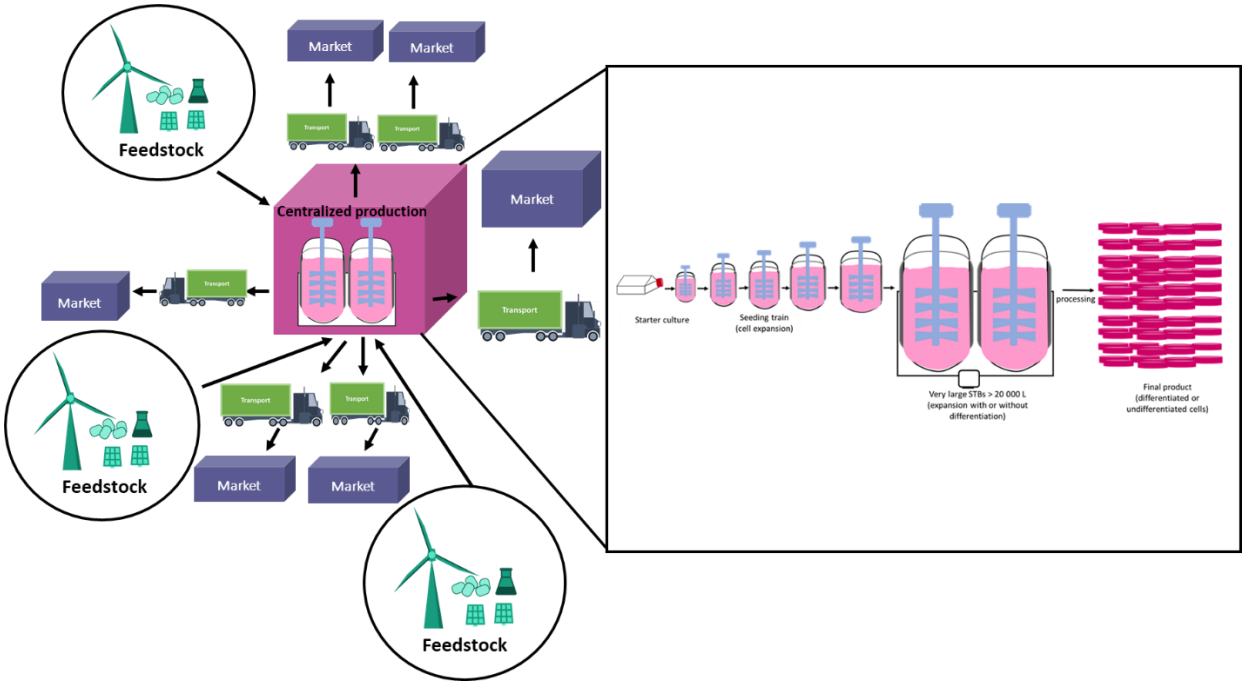

Figure 24: Ambitious industrialization of CM by super larger-scale parallelization for global market

Conclusions and future perspectives

In this report, we have thoroughly examined various aspects of bioreactors for the production of CM/CSF. Our focus has been on identifying critical factors that contribute to the success of the production process, the quality of the final products, and the feasibility of larger-scale manufacturing.

We emphasized the importance of optimizing bioreactors not only for the efficient recovery of biomass as the end product but also for ensuring that the biomass structurally and sensorially mimics traditional meat in terms of texture, flavor, and color. This alignment with consumer expectations is crucial for the market acceptance of CM and CSF.

Key process parameters in the bioreactors including pH, oxygen levels, carbon dioxide concentrations, temperature, cell density, and cell differentiation were also highlighted as pivotal to the optimization process. To enrich our understanding, we conducted a survey among industry players to gather current insights on bioreactor processes and specifications. Although, the response rate for the survey was low we could still obtain valuable information which could be exploited to improve the technology for example most of the companies propose that larger-scale production can be achieved by scaling-out large bioreactors through parallelization which supports our concept of bioreactor parallelization for industrial CM/CSF production.

Based on our review of bioreactor concepts and processes for CM/CSF production, we established key performance indicators (KPIs) aimed at guiding bioreactor design and process optimization. These KPIs are essential for ensuring the efficient production of CM/CSF and should be integral to any development or optimization efforts.

For industrial-scale CM/CSF production that yields substantial quantities of high-quality products capable of competing with traditional meat, we propose a strategy involving the parallelization of bioreactors across different scales. This approach enables flexibility and scalability in production, allowing for adaptation to varying market demands.

However, it is imperative that we further investigate the bioreactor parallelization concepts and conduct a comprehensive life cycle assessment (LCA) analysis across different production scales. This analysis will enable us to identify the most sustainable and cost-effective methods for producing CM/CSF, ensuring that our processes align not only with economic viability but also with environmental sustainability.

In summary, this report emphasizes the need for ongoing research and development in bioreactor technology and process optimization, which are crucial for the advancement and adoption of CM/CSF in the marketplace.

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