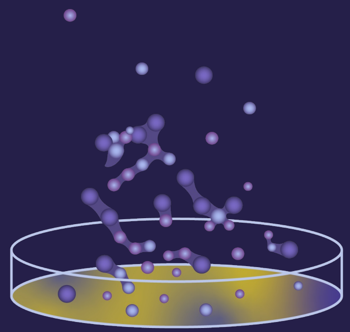
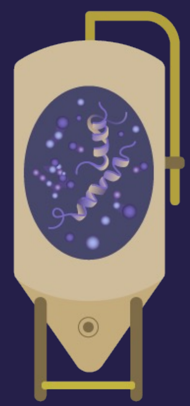
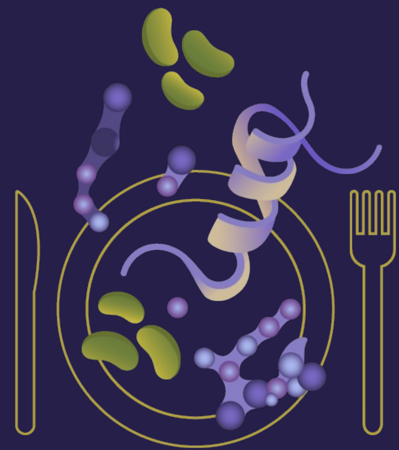




Roadmap

Paving the way towards animal free milk proteins



21st BIO

ProteinFrontiers

NIRAS

Ministeriet for Fødevarer, Landbrug og Fiskeri gudp

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The Network Animal Free Protein –
Fermentation Produced Milk Protein
is supported by GUDP

Ministeriet for Fødevarer,
Landbrug og Fiskeri

Preface

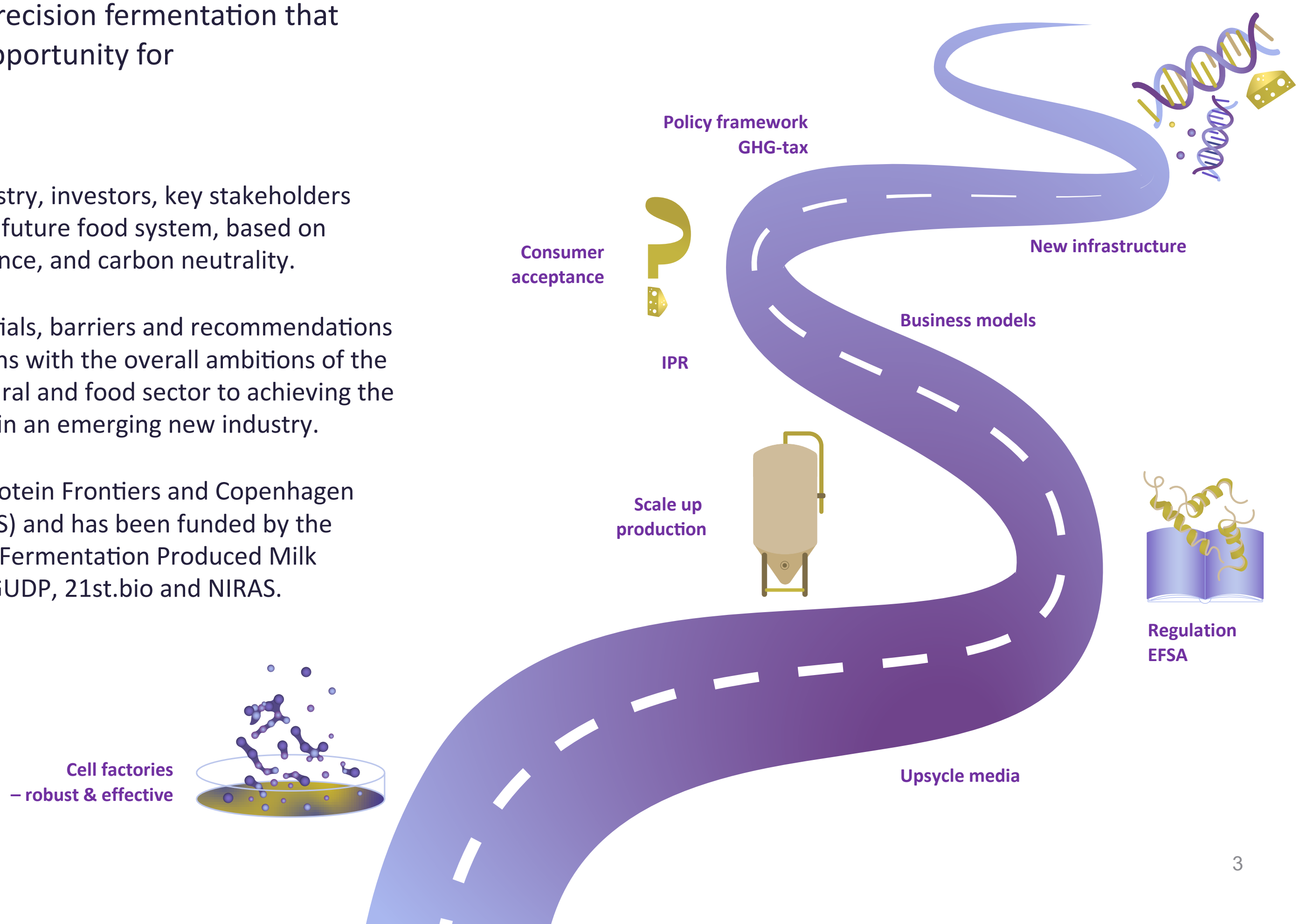
Paving the way towards animal free milk proteins

This roadmap describes the overall steps to establish a precision fermentation industry for milk proteins. The vision is to create a Danish hub for protein food ingredients produced by precision fermentation that will create a new export opportunity for sustainable foods.

The Roadmap shall inspire industry, investors, key stakeholders and policy makers to frame the future food system, based on sustainability, circularity, resilience, and carbon neutrality.

The Roadmap addresses potentials, barriers and recommendations linked to the value chain. It aligns with the overall ambitions of the green transition of the agricultural and food sector to achieving the climate goals and creating jobs in an emerging new industry.

The Roadmap is prepared by Protein Frontiers and Copenhagen Institute for Futures Studie (CIFS) and has been funded by the Network Animal Free Protein – Fermentation Produced Milk Protein which is supported by GUDP, 21st.bio and NIRAS.



Summary

Animal free milk proteins is a global business opportunity that decarbonize the food system

Denmark needs to transform the food system to become climate neutral by 2045.

This requires a significant part of the livestock to be taken out of the equation and replaced by plant-based food, which in part is challenged in terms of taste, functionality, and nutrition. This creates barriers for many consumers acceptance. Animal proteins produced by precision fermentation does not have this barrier. Furthermore, the fermentation processes have a low climate impact, supplements and improve the plant-based diet and reduce CO_2 emission by 50-90pct.

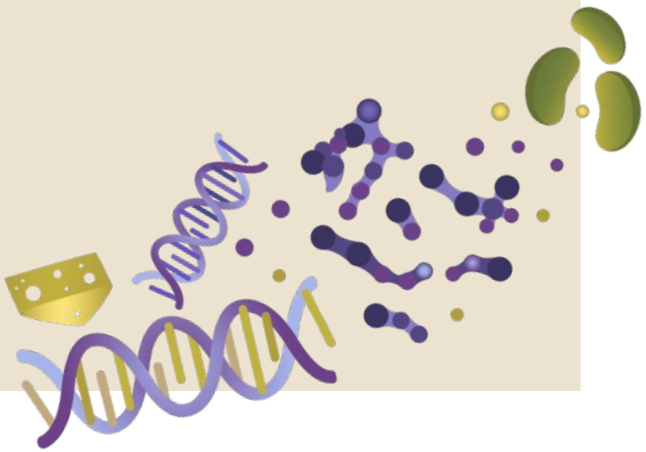
Our shared vision is that Denmark becomes a leading country in the precision fermentation of milk proteins - a country that reduces greenhouse gases, frees up agricultural land, preserves jobs and creates new export opportunities for the food industry.

The technology of precision fermentation is well established in pharmaceutical and enzyme production for the past 40 years. Denmark has a unique position with industrial biotech expertise which provide a competitive edge and comparative advantage in future production of milk proteins for food ingredients.

Precision fermentation radically helps to decarbonize the food system.

The transformation of the food system is expected to happen in 3 waves:

- 2020 - 2030 Plant-based proteins
- 2025 - 2035 Microbially produced proteins (this roadmap)
- 2030 - 2040 Cell culture meat



Summary
The roadmap's key tasks for immediate action

Danish Government should work for:

- EU to modify “Novel Food” regulatory processes, prepare a fast-track model and a GRAS-inspired approach to reduce time to market.
- Push for an ambitious EU strategy for precision fermentation of food that will foster investor confidence to provide CAPEX investment for establishing the new industry.
- Investment in research, development, pilot and demonstration facilities including production infrastructure for startups.
- Subsidies for mitigation and adaptation to climate objectives including carbon taxes to drive market uptake of alternative proteins.
- Setting up targets and timeline for plant-based food and alternative proteins to prepare consumers, markets, businesses and investors.
- Infrastructure planning of the future industrial hubs for precision fermentation –model Kalundborg.

The industry should:

- Create an ecosystem for precision fermentation, optimize the supply chain to reduce cost.
- Establish a feed stock industry based on local agriculture and bio-residuals to supply sustainable production media
- Establish standards and guidelines to ensure consistency, safety and quality of precision fermentation to facilitate regulatory approval. Ex. Harmonized LCA guidelines.
- Build industrial fermentation capacity for bulk production

Civil society organizations should:

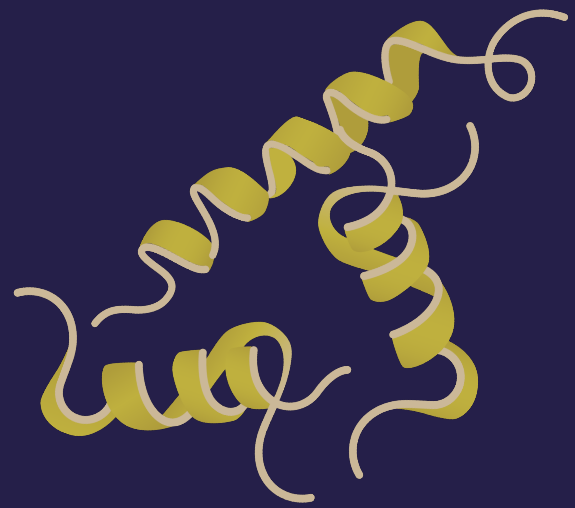
- Inform and create a public dialogue with consumers about precision fermentation of food.

Universities should:

- Establish open innovation platforms where companies, universities and start ups can collaborate on solving common challenges related to precision fermentation of food.
- Develop robust and efficient production organisms to produce on food grade medias based on bio-residuals.

Content

The vision for Denmark

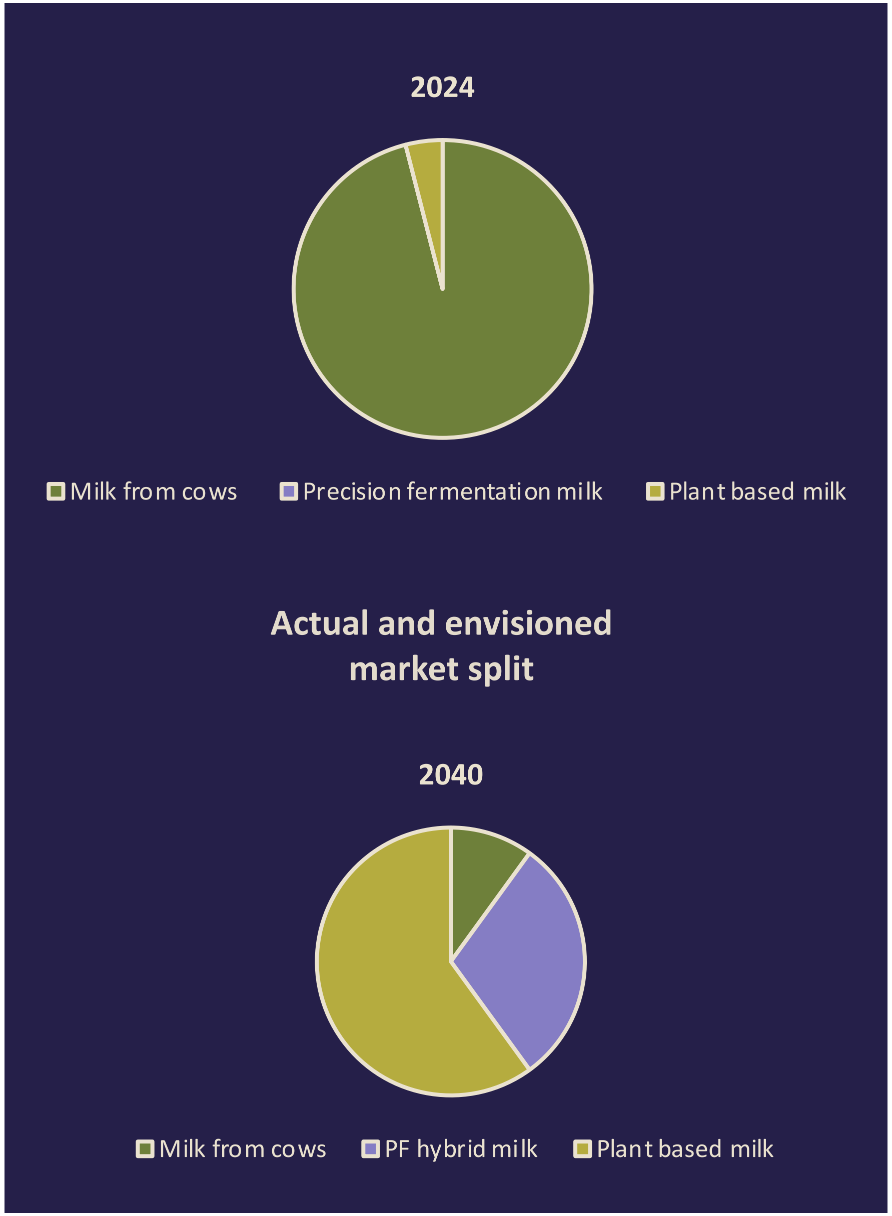


Our shared vision

In 2040 Denmark has become an international leader in precision fermentation of milk proteins with a significant export of non-cow dairy food ingredients.

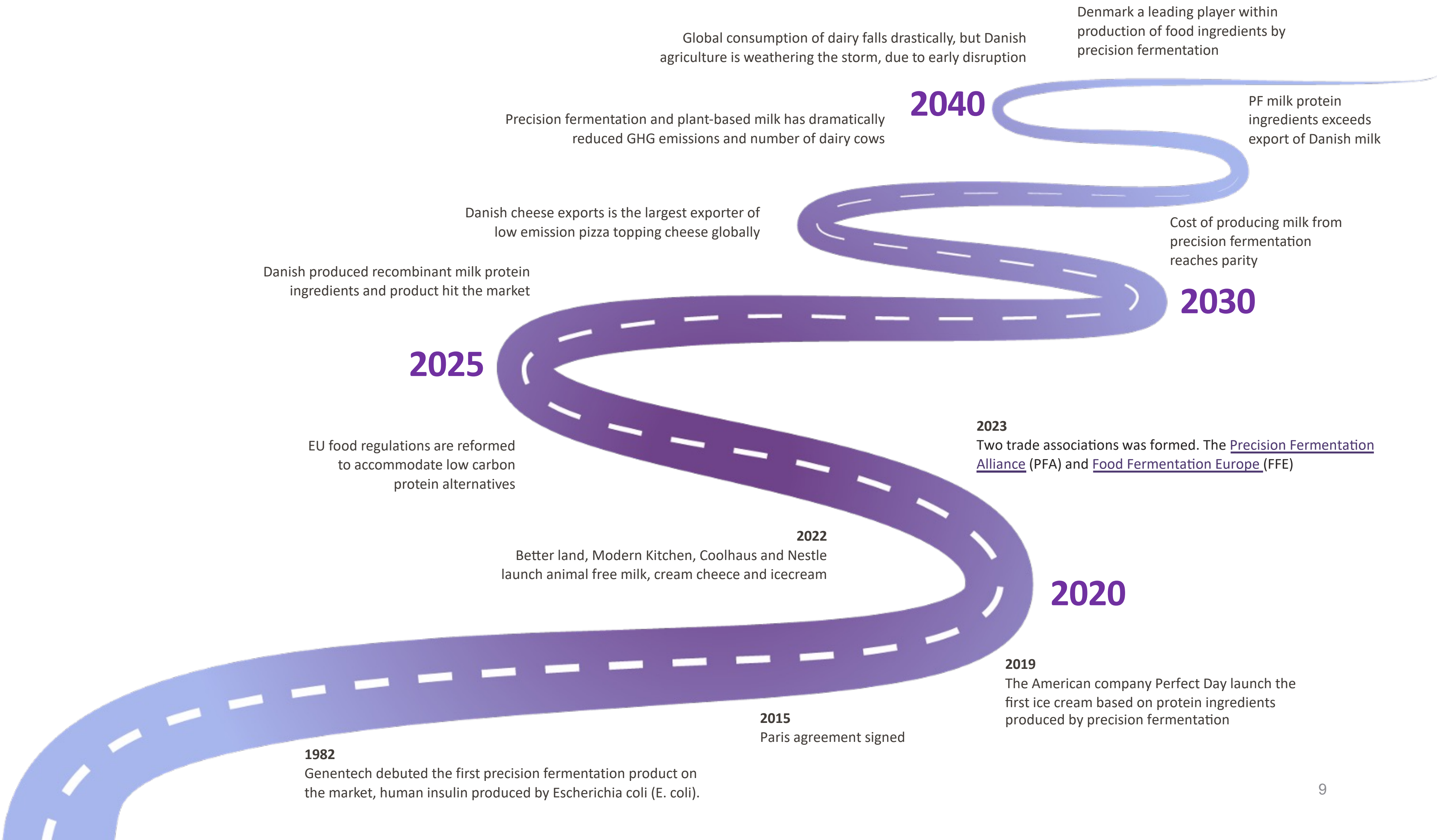
This has been the result of widespread cross sectorial collaboration among universities, biotech industry, government, food and agricultural sector which has enabled the transition. Denmark has become a knowledge hub for precision fermentation of food ingredients attracting Foreign Direct Investment (FDI), start-ups and corporates worldwide. Research institutions are leading in the field of precision fermentation. Denmark is leading the way in modernizing agriculture for a zero-carbon world.

Denmark has become a hub for industrial scale precision fermentation of food ingredients, creating highly paid jobs and export opportunities – a copy paste of the Danish pharmaceutical industry.

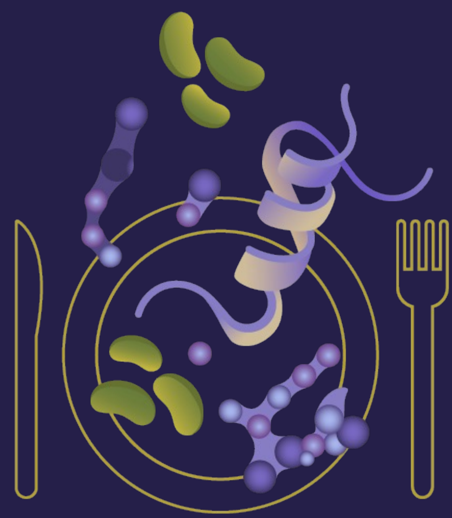


Timeline

Paving the way towards animal free milk proteins



The challenge of the food-future



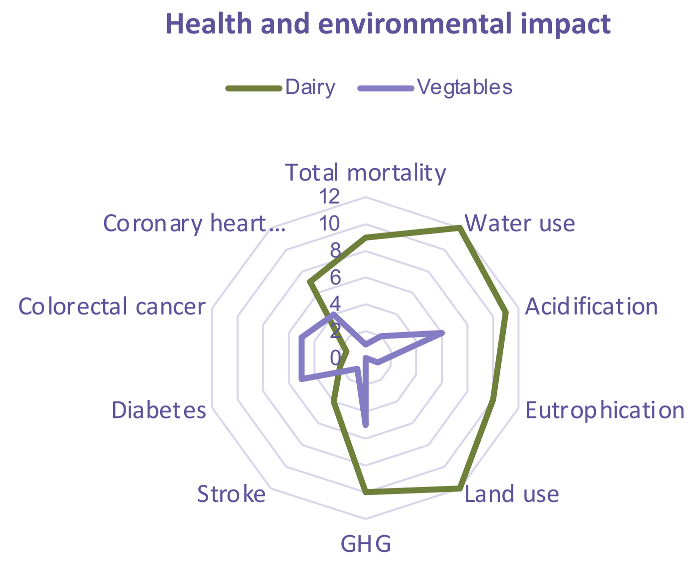
The environmental limitation for dairy

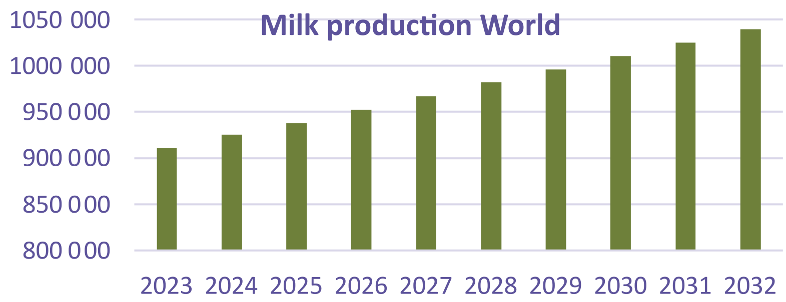
Over the last decade the demand for milk has increased 18% and as the middle class grows the demand for milk proteins will increase.

This has several environmental effects such as the exploitation of land resources to grow feed stock. The expansion of dairy operations lead to deforestation and habitat loss, particularly in regions where forests are cleared for pastureland or feed crops. Overgrazing and improper manure management, can degrade soil quality and create nutrient depletion, affecting long-term agricultural productivity and ecosystem health.

At a global level livestock feed production utilizes 77% of arable land and over 40% of total agricultural water, and run-off of fertilizers and chemicals from crop production can lead to environmental damages to sea and land (UNEP, 2023)

Dairy require extensive land use and given the lack of availability of land this in turn quickly becomes a food security issue.





Source: UNEP, 2023; OECD/FAO (2018),

The challenges for dairy

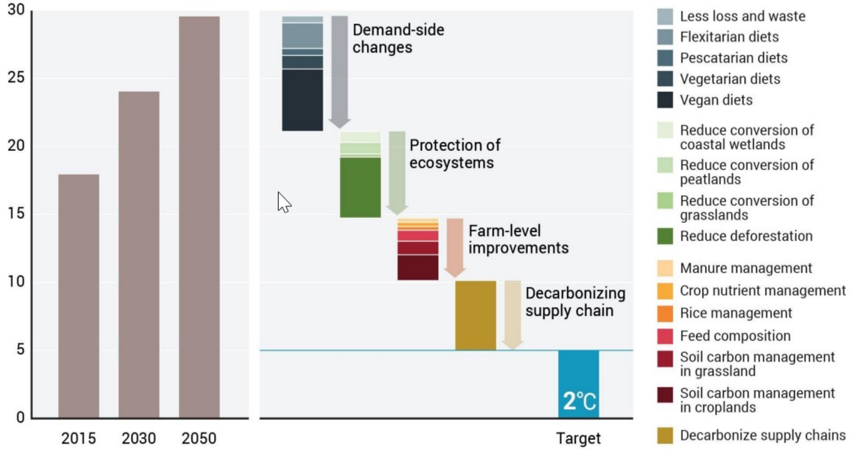
Livestock account for 20% of all human induced GHG emissions predominately from beef production, but dairy also has significant GHG contributions, higher than that of the criticized airline industry (Augère-Granier,2018). Hybrid milk consisting of oat drink and milk protein from precision fermentation can reduce GHG from cow milk between 50-90% (Xu et all, 2021). The more sustainable energy is used in production the less GHG intensive it is. This goes along way to further the shift away from meat and milk-based protein.

According to the UN shifting to a more vegetarian diet is seen as one of the largest contributions factors for agriculture to meet the 2C goal. A vegetarian diet has considerable benefits for the planet as well as human health, but also have considerable long-term benefits for government finances. According to the Lancet Commission on Obesity, the transitioning to a planetary diet, mainly plant-based aimed at feeding the world within planetary boundaries, could decrease global healthcare related costs by approximately 11 trillion USD per year by 2050.

On top of this it increases efficiency in the highly subsidized farming industry, which for years has received basic income support.

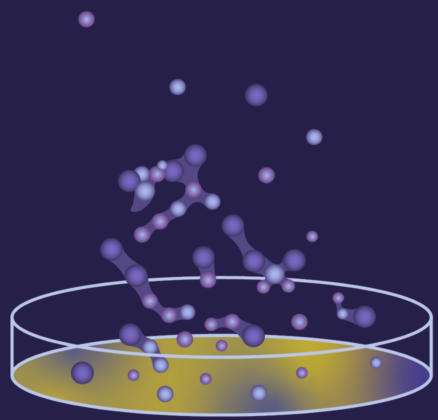
"We cannot solve our problems with the same mindset that created them"
Albert Einstein

Food systems emissions trajectory and **technical** mitigation potentials by 2050



Source: UN Gap report 2023

Introducing
precision fermentation



What is precision fermentation?

The Roadmap focusses on industrial scale protein production by precision fermentation of (beta lactoglobulin BLG and Casein) as a model for broad use of precision fermentation in the food industry.

Precision fermentation is a technology that involves microorganisms like bacteria, yeast, or fungi to produce specific compounds through fermentation. This process allows for the precise control and manipulation of microorganisms' genetic makeup to produce desired products.

In the context of creating alternative proteins, precision fermentation can be employed to produce proteins and other components found in traditional dairy products. This implies identifying the genes responsible for producing the desired components. For dairy, of particular interest are casein and whey proteins since they are responsible for making dairy taste the way it does. Using synthetic biology techniques selected genes are inserted into a host microorganism, such as fungi or bacteria. These microorganisms need a controlled environment where they multiply and produce the desired dairy proteins The target components are harvested and processed to create the final product often a powder to be used as an ingredients in the food industry.

Compared to cow milk the estimated reduction of GHG by using precision fermentation to produce milk proteins is within the range of 50-90%.

Cell Factories

Technology enables precise genome modifications (ex. CRISPR) in microorganisms, allowing synthetic genes identical to those found in cow genomes to be inserted into desired hosts. This technology is increasingly faster and more cost-effective, facilitating the creation of new cell factories.t

Protein Synthesis

Equips microorganisms with genetic information to synthesize milk proteins, akin to brewing beer but yielding milk protein instead of alcohol.

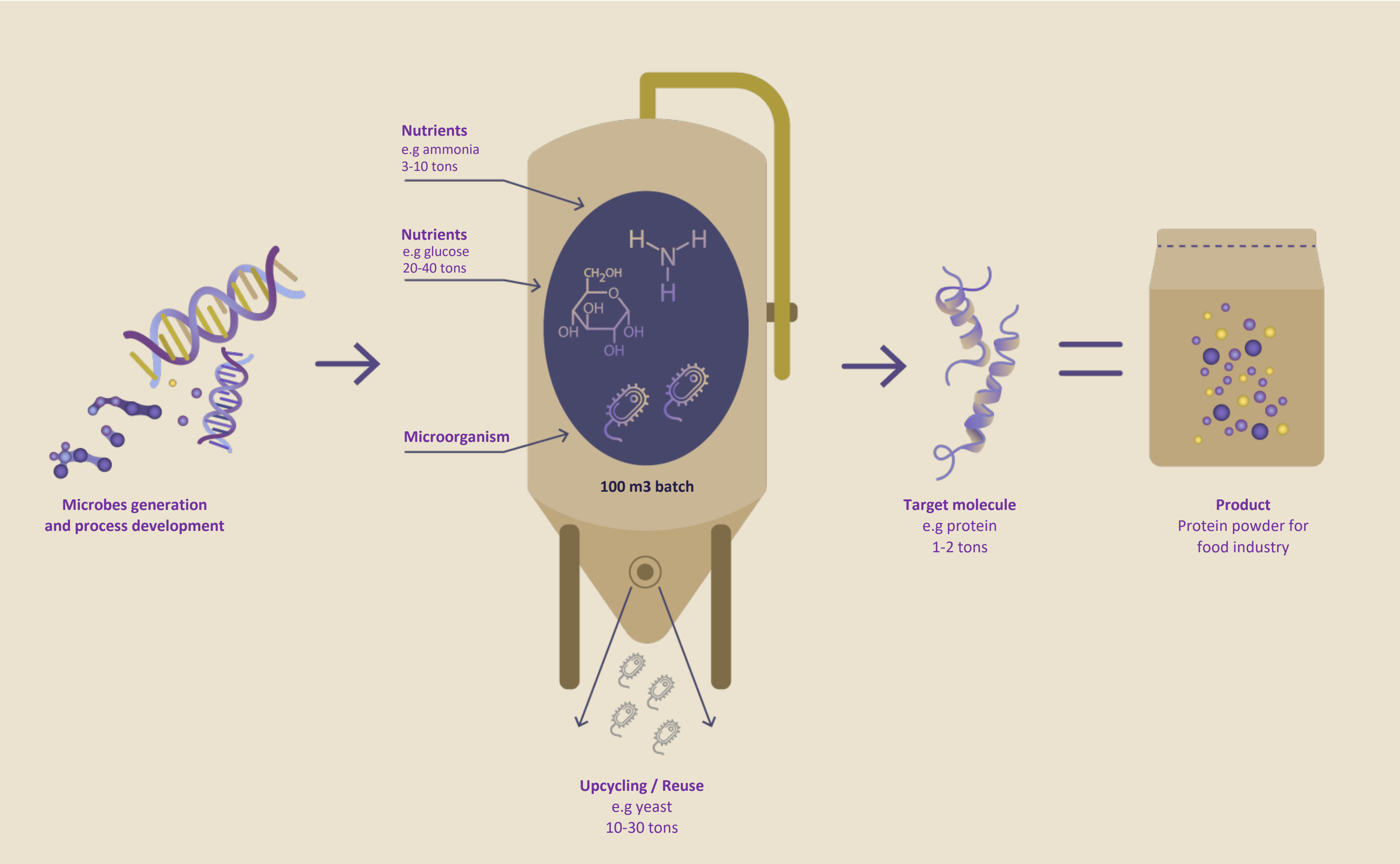
Optimal Growth

Conditions, including nutrients, pH, temperature, and oxygen, are essential for producing milk proteins.

Final product

Proteins are harvested to create final product Non-GMO processes involve screening naturally occurring organisms to produce proteins resembling those from animal-produced milk.

What is industrial scale precision fermentation of proteins?



The solution

Cows can’t produce milk proteins without methane emissions – microbes can!

Creating alternatives to dairy proteins is faced with a range of challenges.

- The taste and texture of milk is enjoyed by millions across the world and habits are hard to break.
- Dairy have functional qualities that make it versatile and is used in a wide range of foods from pizza to steamed foamy milk.
- Dairy provide nutritional content and the protein is easily digestible by our bodies (unlike the protein in plant-based milk) making it part of many governments' dietary guidelines.
- Cow's milk contains micronutrients such as calcium, B2, B12 and to a lesser extent phosphorus, magnesium and zinc. Cow's milk is an important nutrient source for many people. This must be addresses by alternative dairy.

The lack of protein in plant-based milk has created a push back from authorities in the USA due to existing health guidelines. However, in the EU and the USA, people are generally getting enough protein, but in a world that is shifting to more plant-based diet and reducing meat consumption, having a plant-based milk high in protein such hybrid milk, would be beneficial. Precision fermentation can produce beneficial proteins like Lactoferrin in concentrations as high as human breast milk for infant formulas. A hybrid milk also has the benefit that 68% of the global population is intolerant to lactose which is found in ordinary milk, but not in hybrid milk (Carr et al, 2021). To top it off it reduces land use, limit problems with antibiotics resilience, and is environmental and animal friendly.

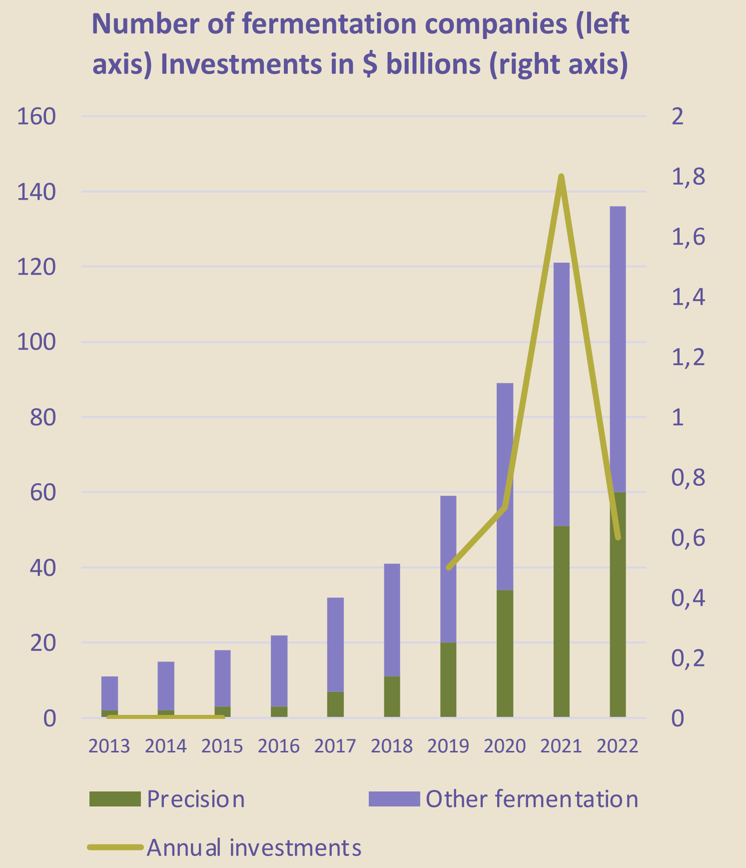
“A hybrid milk also has the benefit that 68% of the global population is intolerant to lactose which is found in ordinary milk, but not in hybrid milk.”

The status of the precision fermentation industry

The precision fermentation industry for milk protein is rapidly advancing.

Several companies are making strides in producing milk proteins like casein and whey proteins by fermenting microorganisms like yeast or bacteria with specific genetic modifications used in creating animal-free dairy: milk, cheese, and yogurt as well as functional ingredients for various food applications. Dairy dominates the precision fermentation start-ups.

The first precision fermentation product to reach the shelf was ice cream by ”Perfect Day” in 2019 since then Remilk, Formo, Nutropy and others have joined. Major players such as Danone and Nestle have also started investing in animal free dairy. It’s still early stage of the industry and a lot can change. When asked about which region would take the lead, respondents in the expert panel on precision fermentation generally agreed that the USA had favourable conditions due to access to investment capital, and a better regulatory environment. There are over 20 companies in Europe focused on precision fermentation, but there is still no product on the EU market due to strict food regulations. Respondents in the expert panel also emphasized that Denmark had the know-how to take a leading position, but that it would take government commitment and a strong aspirational vision for Denmark.



Source: Good Food Institute, 2023:

Consumer products containing whey protein (precision fermented BLG) US market - examples

The Biotechnology Race

The technology race

”If you don't disrupt yourself, somebody else will“
Harvard Professor, Clayton Christensen

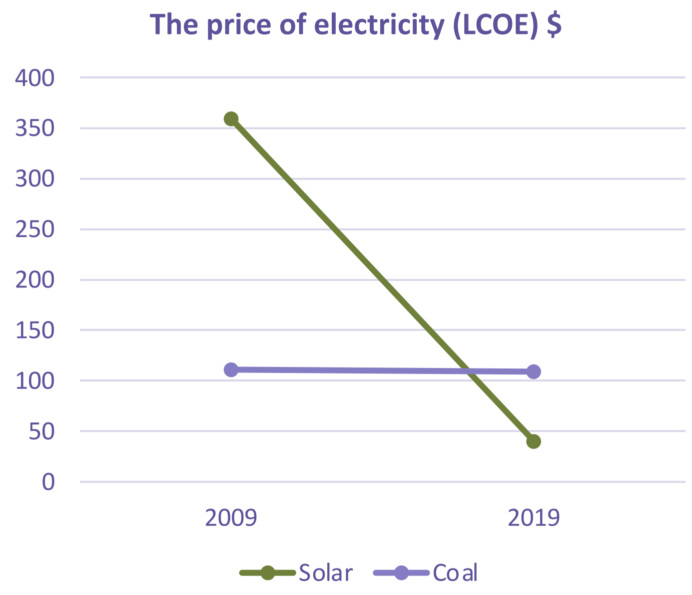
Once the horse was the main means of power, now machines can do the jobs of 100 horses. Technology development is relentless and unstoppable, jobs are lost, but new once appear and ultimately this creates higher productivity and greater prosperity.

Evidence of this technology transition is exemplified by the significant price reduction in solar energy vis-à-vis the relatively stagnant cost curve of coal energy. A decade ago, solar energy was priced at three times that of coal, indicating an unmistakable trajectory favouring solar energy over its fossil fuel counterpart.

The cow like the horse can be seen as a production technology. But like the horse there are natural limits to how efficient a cow can be.

The same way solar is outcompeting coal, the same way precision fermentation will outcompete the cow, it's just a question of time.

According to the expert CIFS survey(2024) on precision fermentation 42% of the respondents believe that the development will be disruptive and if so business and farmers will have a very hard time transitioning, stranded assets and destroyed livelihood could be a result. This underscores the importance of preparing dairy farmers in adapting to emerging technologies.



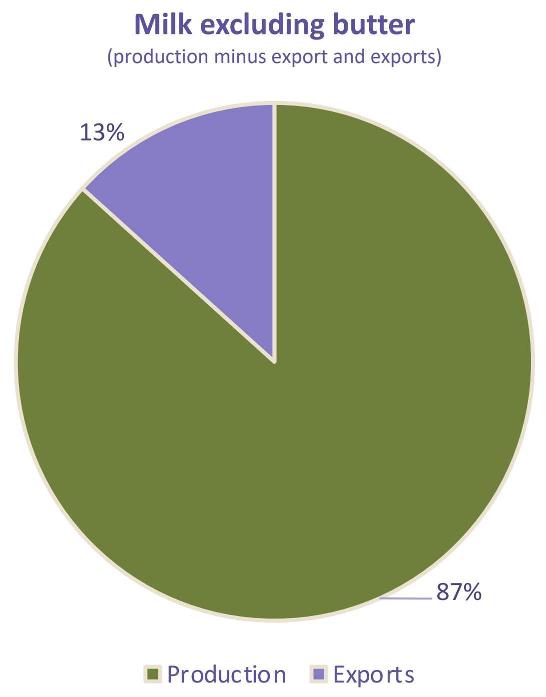
Source: World in Data

Market potentials

Precision fermentation isn't merely about substituting milk proteins. It entails a fundamental transformation of the industry, transitioning milk production from agricultural commodity to industrial manufacturing that is marked by global scaling and consolidation.

The global agricultural dairy market predominantly serves domestic markets, with only 13% of milk production exported. This stands in stark contrast to global markets for manufactured goods, where a handful of global players dominate. It's plausible that milk proteins could similarly be monopolized by a few global market players.

Predicting the exact share of the dairy market that precision fermentation will capture remains premature. However, it's noteworthy that for every 1% Denmark captures of the global dairy market by 2035 through precision fermentation, it secures a market worth DKK 122 billion[2]. To put this in perspective, the entire global diabetes drug market was valued at DKK 553 billion in 2023[3]. Even if precision fermentation were to capture just 10% of the dairy market by 2035, it would still surpass the size of the entire diabetes market in the same year.



Source: 1) OECD FAO, Capital Group 2018, (table), 2)CIFS based on Allied Market Reseach 3)fortunebusinessinsights.com

Cost expectations

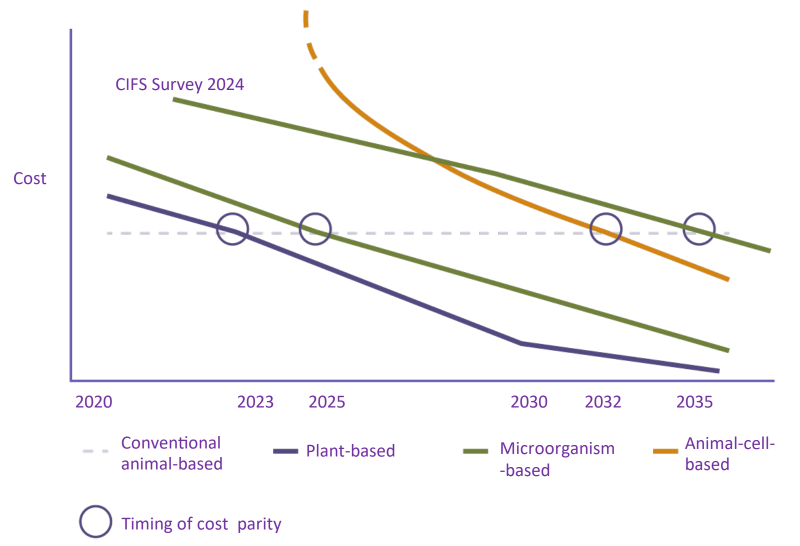
Cost of precision fermentation is high today and only few products are on the market.

For precision fermentation to be a serious alternative to conventional dairy it must be competitive on price, since there is low willingness by consumers to pay extra for animal free dairy(Banovic et al., 2024) . The breakeven price for precision fermentation should be considered the dairy price including carbon taxes.

In the precision fermentation survey (CIFS 2024) experts were asked how much the cost of precision fermented bulk milk protein will have fallen in 10 years' time. The responses converge around 40-60% . The CIFS expert panel believed in price parity around 2035.

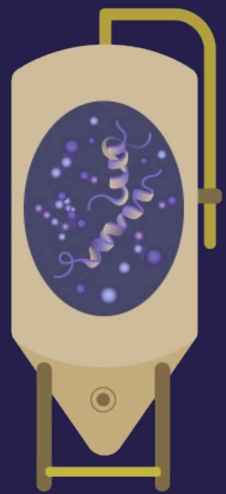
Nestlé has recently debuted Better Whey, a precision fermentation dairy protein powder at a cost of $2.3 per ounce roughly double that of their brand's plant-based whey and dairy based alternative. Taking these prices as starting point and taking the assessment of the expert into consideration the precision fermented Better Whey product would be market competitive in 2035.

Relative timing of cost parity for alternative proteins with realistic taste and texture



Source: Boston Consulting Group, 2021: Food for Thought - The Protein Transformation; CIFS, 2024

Danish strongholds



Actors in the value chain and Danish strongholds

Synergetic opportunities

R&D, Scaling | Upstream | Manufacturing | Distribution

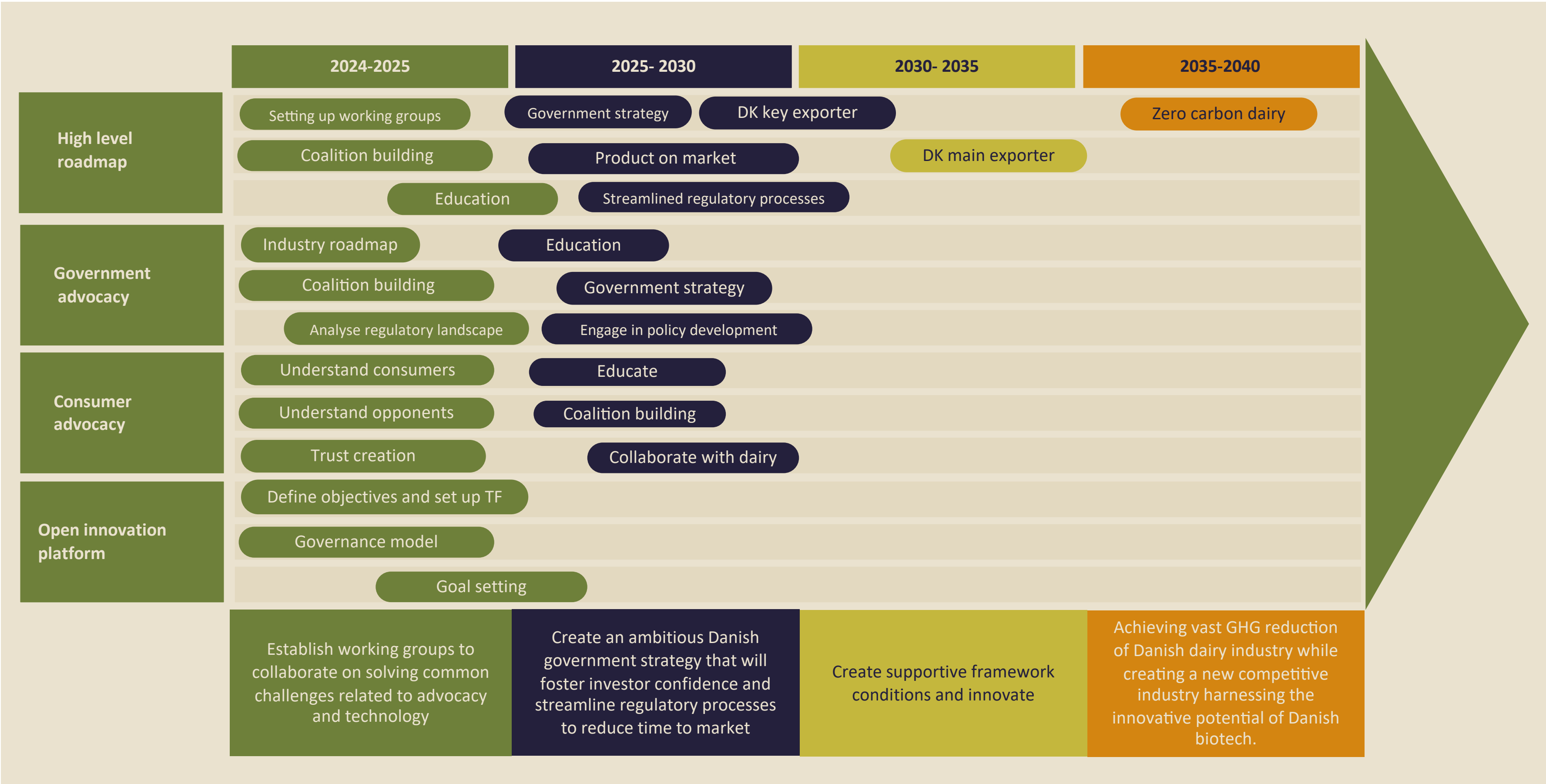
	Synergetic opportunities	R&D, Pilot scaling	Upstream Raw materials input; B2B	Manufacturing, Process control B2B	Distribution/ B2C
Institutions	Networks and NGO's: Food and Biocluster Denmark, Plantebranchen, PlanteVærket, Netværk for Fremtidens Planteproteiner, Planteindustrien, Dansk Naturfredningsforening, Dyrenes beskyttelses, Rådet for Grøn Omstilling, Concito	Research Institutions: KU, DTU, Aarhus Uni, Aalborg Uni, Teknologisk Institut, FermHub	Farmers Industry: Novonesis, Harboe. DLG, GEA, TetraPak Networks: Food & Biocluster Denmark,	Manufacturing: Novonesis, IFF, Unibio, Arla Foods Ingredients Process control and instruments: NIRAS, GEA, TetraPak, 21st.bio	Distribution: COOP, Salling Group Consumer brands: Remilk, ARLA
Strongholds	The Danish government has a clear target of reaching zero carbon by 2045 an ambitious target that will require huge adjustments in agriculture. This has created and continues to create a wealth of organisations that are trying to work together to reach this goal, that provide synergetic opportunities for the roadmap participants.	Denmark boasts world-class research institutions and universities that are at the forefront of biotechnology and food science. These institutions provide a fertile ground for cutting-edge research in precision fermentation techniques for dairy proteins. Further investment from Danish government in research and innovation and collaboration between academia, industry.	There is a strong emphasis in Denmark on creating a more circular economy with a strong push towards a greater integration of energy, agriculture and waste. Precision fermentation with into this mix, with is focus on upcycling waste materials using biotechnology.	Denmark is home to numerous biotech companies with expertise across the entire value chain of precision fermentation. These companies specialize in fermentation technology, process optimization, and product development. With a strong emphasis on innovation and entrepreneurship, Danish biotech firms could drive the commercialization of animal-free dairy products on a global scale.	Danish consumers generally show positive attitudes towards initiatives helping to reduce climate change. Denmark is a country that has often been used by major brands as a test bed for product launches and so would be a good place for major brands to launch precision fermentation product.

The TOWS analysis allows you to think about strategies around the internal and external areas

(TOWS - Threats, Opportunities, Weaknesses, Strengths)

TOWS	**Strengths** •Very powerful research and development capacities •Leading biotech industries, with many global players with expertise across the value chain •Climate awareness •Strong entrepreneurial environment	**Weaknesses** •Lack of investment, compared with US: difficult to attract high-risk capital •A conservative and strong agricultural lobby •Expensive labor, very high taxes •Low political focus, lack of vision/long term strategy •GMO fright •Large percentage of population who do not wish to change consumption •Lack of infrastructure for upscaling •EU regulations on GMO and novel foods
Opportunities •Reducing CO2e from agriculture •Helping to achieve food security and reduce food related conflict •Helping to increase animal welfare •Creating a competitive Danish agricultural and biotech sector •Helping Danish dairy farmers to transition in time to avoid major disruptions	**SO strategy** •Making politicians aware of the climate benefits •Create industry collaboration to optimize the supply chain to reduce cost •Establish open innovation platforms where companies can collaborate on solving common challenges related to precision fermentation •Allocate soft funding for startup environment	**OW strategy** •Create an ambitious Danish government strategy for precision fermentation that will foster investor confidence. •Work together to establish industry standards with clear guidelines to ensure consistency, safety and quality of PF to facilitate regulatory approval. •Collaborate on advocacy efforts, a unified industry voice can have a strong impact on policy development
Treaths •The USA have risk willing capital a more lenient regulatory environment. The USA could easily get a head start and win the game.	**TS strategy** •Create an ambitious Danish government strategy for precision fermentation that will foster investor confidence •Streamline regulatory processes for precision fermentation products to reduce the time and cost associated with bringing these products to market	**TW strategy** •Streamline regulatory processes for precision fermentation products to reduce the time and cost associated with bringing these products to market •Establish open innovation platforms where companies can collaborate on solving common challenges related to PF

Danish roadmap
Overall timeline for action
– precision fermentation produced milk proteins



Danish roadmap

Timeline for government advocacy

- Roadmap and coalition building: Collaborate with industry, NGO's and other stakeholders securing broad commitment and ownership of the process to form coalitions centred around a roadmap to propel action forward, leverage collective expertise, resources, and influence to advocate for common policy objectives and mobilize support from a broad range of stakeholders. Task: 1. Create industry roadmap with a vision that can be supported by stakeholders. 2. Secure resources and funding and create a steering group potentially a secretariat if funding allows. 3. Create a strong coalition by identifying initiatives that have synergies with the roadmap such as the parties involved in the Danish action plan for plant-based foods.

- Analyse regulatory landscape: Analyse the existing regulatory framework and the history and purpose behind it. Identify key stakeholders affecting policymaking and regulation and identify stakeholders with common interests: NGOs, corporates and politicians. Examples of aligned goals could be reducing GHGs, securing jobs in a ripe for disruption sector, enhancing animal welfare.

- Relationships and education: Establish relationships with policymakers and relevant stakeholders at national and EU level. Provide policymakers with accurate, balanced information about the benefits of PF, potential risks, and societal impact. Proactively address potential concerns by policymakers, NGO's, industry lobbyists.

- Government strategy: Partake in developing an ambitious Danish government strategy for precision fermentation that will foster investor confidence by providing a clear signal to the market about Danish commitments.

- Engage in policy development: Participate actively in the policymaking process by submitting comments, proposals, and recommendations to regulatory agencies and legislative bodies to shape favourable outcomes for precision fermentation technology and market creation. This should include recommendations for regulatory reforms to streamline regulatory processes to reduce the time and cost associated with bringing products to market. Engage both nationally and in the EU to speed up EFSA approval, promote innovation, competition, ensure interoperability, IPR, and enable fair market access.

Danish roadmap

Timeline for consumer advocacy

- Understand consumers: Barriers for adoption needs to be understood thoroughly these include benefits to consumers, pain points, willingness to pay, as well as scepticism and potential misunderstandings they might have. How can information alleviate some of the technology concerns they might have? Different audiences need to be identified. What are the preferences of early adopters vs early majority, identifying this may overcome the innovation chasm?

- Understand opponents: Understand the arguments that will arise from industry lobbies and how they will try to address the public, including politicians. Is there a common ground that can be found in order to have a constructive dialogue?

- Trust creation: Create credibility by setting up an independent advisory board consisting of a respected unbiased group of researchers.

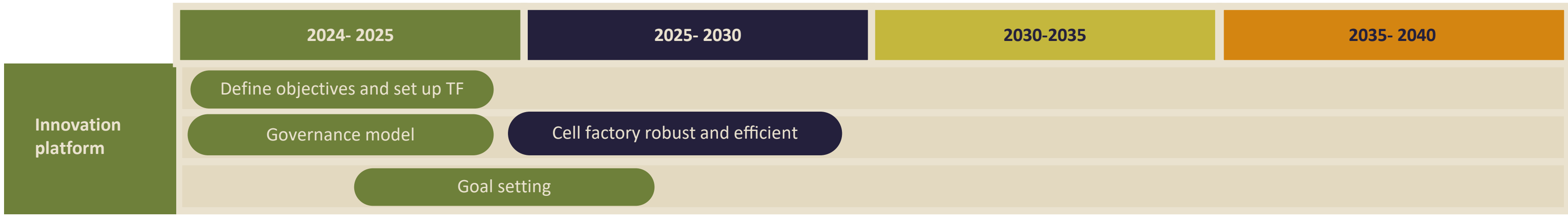
- Educate and Inform: Develop educational content to inform specific targeted consumer groups, the wider audience and identify the weak spots in opponents' arguments. Disseminate information through appropriate channels. Showcase benefits, practical real-life stores from consumers as well as science backed data on the wider societal benefits. Engage with consumers and address concerns and misconceptions. Maintain openness to uncertainty and create transparency in communication to build trust. Acknowledge the potential downside this may have to dairy farmers and engage constructively in dialogue.

- Coalition building: Collaborate with NGOs and corporates that are trying to meet the Paris agreements.

- Collaborate with dairy farmers and associated organisations: Dairy farmers will have reservations concerning precision fermentation. They need to see themselves as part of the solution. Work together to support dairy farmers in creating a just transition.

Danish roadmap

Timeline for open innovation platform



- Define objectives: Understand the main challenges that needs to be tackled. Make clear problem definitions and set up task forces potentially with cross cutting task forces aimed at solving shared problems with the aim to accelerating innovation. Clearly define which challenges are suitable for an open innovation platform and what challenges stakeholders prefer not to collaborate about.

Example of task forces:

1. Develop industry standards
2. Achieve robust and efficient cell factories
3. Production medias
4. Industrial scaleup challenges

- Governance model: Develop a play book, so that each party understands the conditions under which the open innovation platform will operate. This includes rules for participation, expectations for collaboration, and protocols for sharing resources and knowledge as well as outlining the roles, responsibilities, decision-making processes, and mechanisms for managing conflicts and disputes among stakeholders. This model should also address issues such as intellectual property rights, data sharing, and confidentiality.

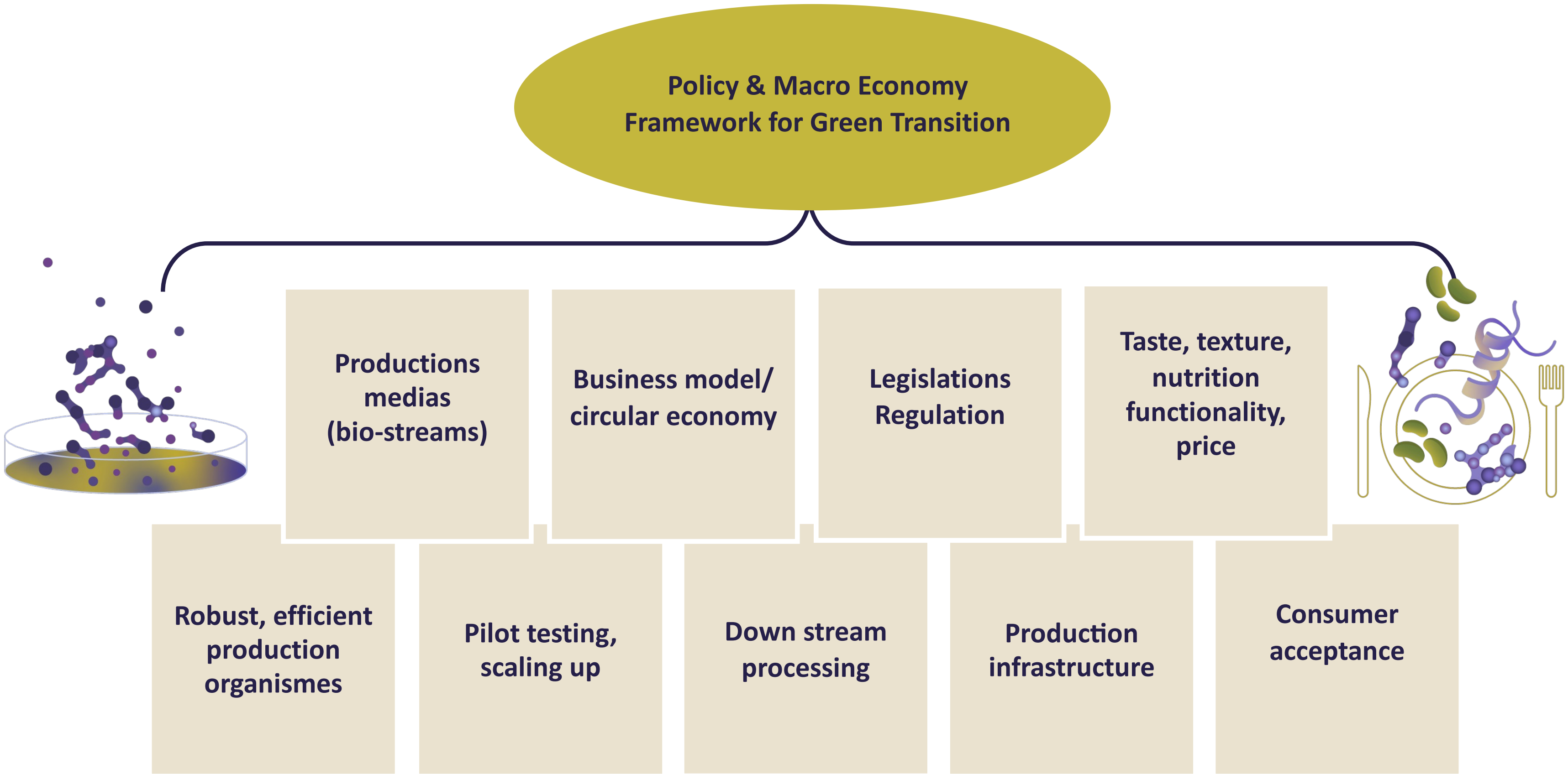
- Goal setting: Have each task force revisit objectives and set clear targets and define role and responsibilities.

- Achieve robust and efficient cell factories, solve scale up challenges and challenges related to efficient production medias based on local residual bio-streams.

Barriers and opportunities across the value chain

Value chain

The success of fermentation produced milk protein's depends on achievements in every link of the value chain.



Robust and efficient production organisms – cell factories

Microbes will most likely supplement and replace some of the traditional livestock. Precision fermentation allow us to produce animal identical ingredients such as proteins, fatty acids, vitamins etc. with a very low climate and environmental impact.

Potentials

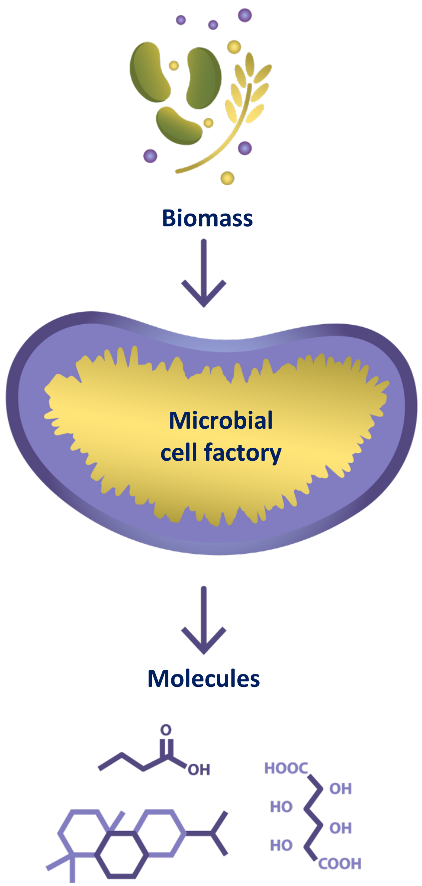
- Increasing concentration, also known as titer, is key for industrial mass production of precision fermentation of milk protein. There is a direct proportionate relationship with titer, and the cost of unit sold (COGS). The rule of thumb, when titer doubles there is a 2x decrease in COGS.
- A range of optimizing areas to increase titer, is being explored. Finding better microbial strains and tailored growth media to provide essential nutrients. Different strains have different capabilities in terms of protein production (titer -g/l efficiency) and robustness of the microbe.
- It's important to find ways to overcome side-products (ex. Acid) in production that might interfere with the fermentation process and reduce the efficiency of protein production, it is important to have a reliable production.
- Products need to be assessed to ensure they are suitable for food and mass production.

Barriers

- IPR – there is a global race to control IP on cell factories.
- Massive engineering needed to produce milk proteins recombinantly - (counter act degradation, increase yield/titer, get PTMs right, co-expression, close knowledge gaps)
- Screening platforms are lacking (HTP protein detection platforms; HTP tools for fungi)
- Developing standard protein functionality tests are needed for working with protein production
- Precision fermentation production of food is the shift from a pharmaceutical model, which high value target protein, to a food model, which emphasizes high volume at a lower value. It is a challenge to make a business case for food.

Recommendations

- Denmark has cutting edge bioengineering in major companies ex. Novonesis and universities such as DTU. It is important for minor companies/startups to have open access to cutting edge bio-technology.
- The functionality of precision fermented proteins is essential. Danish Universities need to have this expertise.



Sustainable production media
– bio-streams, circular economy

Sustainability and reduction of climate impact are important arguments for replacing animal-based food with precision fermentation. A key to sustainable and low-cost production is the upcycling of waste products from industry and agriculture such as spent grains from brewers, spent yeast, wheat straws, potato pulp, apple pomace, molasses from sugar production and in the future "brown" juice from grass leaf protein production.

Potentials

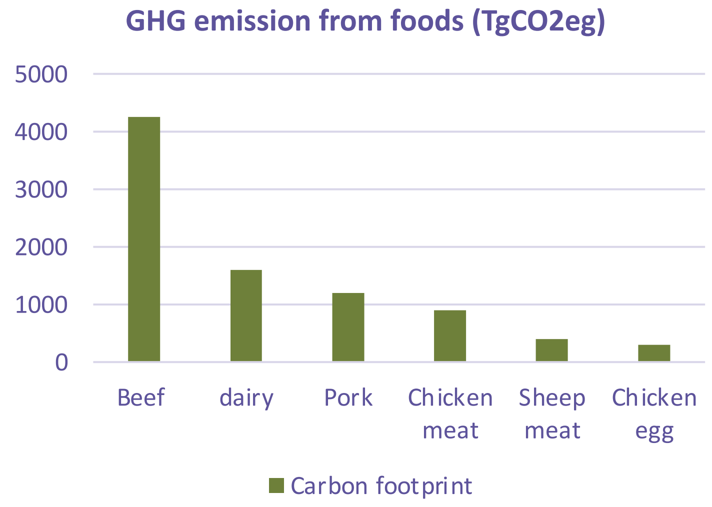
- The carbon footprint of cultured milk (with 3% precision fermented milk protein and 97% oat milk) is less than half that of conventional milk, offering significant environmental benefits. To make precision fermentation of food even more sustainable, production requires renewable energy, the utilization of bio-waste streams, and the efficient use of byproducts in growth media (cascade utilization). Production media play a crucial role in achieving high titers and maximizing the efficiency of the fermentation process.
- The eventual phase-out of the combustion engine in transport will free up a large quantity of corn and sugar for precision fermentation.

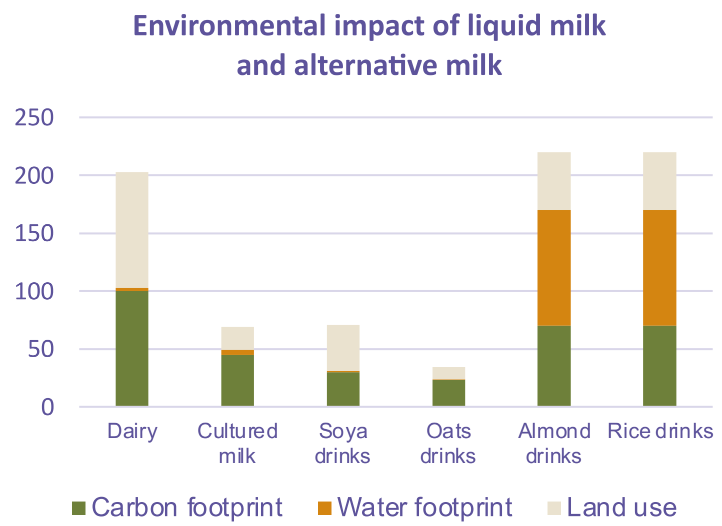
Barriers for using biostream-based media

- Media must be balance between carbon and nitrogen sources, minerals, and antifoams as well as other growth factors:
- Buffer capacity because the media must be able to maintain a stable pH, which is crucial for the growth and metabolism of microorganisms.
- Avoidance high viscosity and foaming that can cause problems in the fermentation process.
- The medium must be free from toxicity and any contamination that could interfere with the fermentation process or be transferred to the final product.
- Consistency must be uniform and support the growth of the organisms, while the medium must technically be manageable in the process plant.
- High quality waste streams must be available throughout the year or be able to be stored for later use

Recommendations

- Denmark must create an ambitious roadmap that target the establishment of a feed stock industry based on local agriculture and bio waste streams to supply sustainable media for fermentation industry of bulk food.





Source: Tuomisto, 2024

Scaling up production

With 40-50years of experience in precision fermentation of pharma and enzymes, significant progress has been made in the lab, including the development of new molecules and genetic strains. However, the primary barrier to broader adoption has been biomanufacturing costs.

Except for pharma, whose business models are mainly built on high-margin, low-volume products with low sensitivity to costs, precision fermentation and biomanufacturing have not yet proven economically viable at commercial scale. Food, on the other hand, operates with lower product prices. Currently, precision fermentation is primarily utilized for niche, high-value projects. Scaling up must proceed incrementally. Denmark has shared scale-up facilities at DTI, 21st.bio and FermHub that reduces CAPEX costs and investment risks.

Potentials

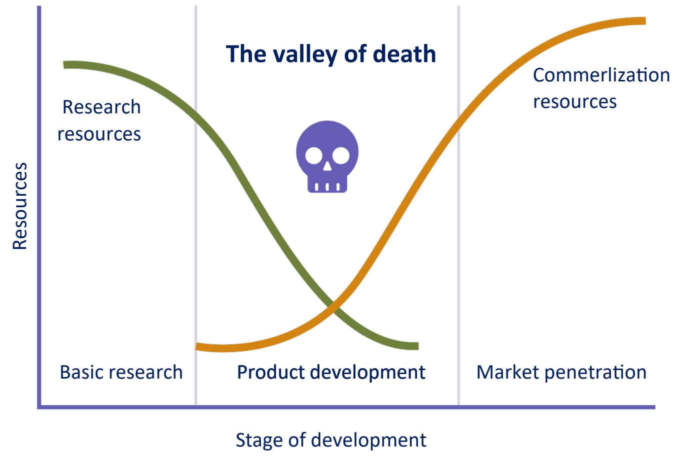
- Despite the inherent challenges in scaling, the surveyed expert in precision fermentation remains optimistic that commodity-scale production will be attained.

Barriers

- The downstream processes, which involve the purification of the target compound and the removal of any trace GMO organisms, are costly and require optimization.
- The existing market is small getting investors to invest in Next generation facilities requiring upfront capital investment of $300 to $400 million that can take 3-5 years to complete each is difficult (BCG, 2024). This is the “Valley of Death” issue.
- Food production requires low unit costs and high volumes, unlike pharmaceuticals, which are higher in cost. Without a lucrative niche market to drive development expenses, the challenges of the "Valley of Death" become more pronounced.
- Scaling need to go hand in hand with reduced climate impact and reduced use of resources
- Process optimization needs to be achieved while transition from small-scale bioreactors to mass production. This involves controlling the fermentation process at scale to maintain process stability and consistency requiring advanced monitoring, real time data analytics and process control for e.g. pH, temperature, dissolved oxygen, and nutrient levels.

Recommendations:

- Provide funding for build scale up, pilot and demonstrations facilities for startups in Denmark
- Stimulate commercial demand to underpin investments; for example, implementing market-pull regulations such as mandatory blending requirements, known from transport sector, such as the biofuels blending mandate.
- Create a Government roadmap with long-term plans to foster investor confidence



Legislation and regulation
- Novel Food

The Novel foods regulation has proven a barrier for alternative proteins such as proteins coming from cultured meat, insects, plant-based proteins and precision fermentation. The aim of the legislation is to ensure that the new products are as safe as existing foods which they are intended to replace. Depending on the strategy of the applicant approval can be sought for the crude protein product (e.g. casein) or for the final food (e.g. a milk-substitute drink) and for use in specific food categories, e.g. milk products or cheeses. With the authorization a decision is also made on how the food should be labelled.

Potentials
The EU has strong competencies within biotech and has created very ambitious targets for climate mitigation. There are huge potentials for European business to help the EU met its political targets, if regulations are facilitating and not a hindrance to unlock the potentials of European Innovation.

Barriers:
- Complex and difficult approval procedures
- Long timelines –approx. 1-2 years
- Costly to provide scientific documentation needed for an EFSA approval.
- The products are not allowed in organic food production as they are considered GMO.

Recommendations:
- Streamline regulatory processes to reduce time to market, make a fast-track model and a GRAS-inspired approach.
- Recognize environmental and climate impact
- Europe must speed up the regulation of bio-based industries to maintain production in EU.

EU Regulatory framework
- General Food Law EC Regulation 178/2002,
- Food Information to Consumers EU Regulation 1169/2011,
- Novel Food EU Regulation 2015/2283,
- Genetically Modified Food and Feed EC Regulation 1829/2003,
- Directive on Contained Use of Genetically Modified Micro-organisms EC 2009/41,
- Qualified Presumption of Safety List - so-called QPS List.

Source: (Vegan Food Law, 2024)

According to EU legislation, food produced by genetically modified micro-organisms in closed tank systems (contained use) is not subject to the rules on authorization and labelling with GMOs, provided that the micro-organisms are not present in the final food (in this case the protein powder).

Sustainable industrial scale production

Scaling up production goes through phases from lab scale to demonstration facilities and further on to industrial scale that can supply the mass market. To met the food market and achieve unit economics that are suitable for the low-cost food market, facilities need to be large still. These facilities needs to be capable of producing + 2 million liters.

Potential

- Contract Manufacturing is very much aligned to serve the pharmaceutical industry, which is a high value product business, and so existing facilities are seldom suitable for the industrial scale that is needed for precision fermentation, instead facilities that are purposely designed, standardized, and optimized for efficient production of milk proteins will be required according to a BCG analysis such standardized biofoundries can reduce the capital investment for biofoundries by up to 30% (BCG, 2024).
- Large-scale industrial production of proteins through precision fermentation is highly compatible with collaborative efforts involving other companies. By incorporating residual waste streams from various industries, this approach aligns effectively with the principles of the circular economy and is ideally suited for fostering industrial symbiosis.

Barriers

- As production facilities grown larger and batches exceed 100.000 liters new problems arise that are not necessarily the same as with lab facilities. This might require different strains and processes than for lab facilities.
- Ruined batches in large 100.000 liters fermenters are very costly requiring standardized processes and process control.
- Testing and performing research on large scale facilities, with different properties than lab scale, with high batch cost is very costly.

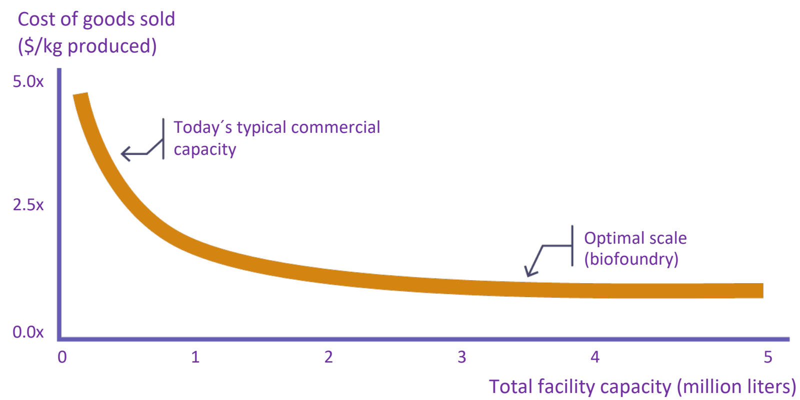
Recommendations

- Initiate the planning process for the establishment of potential new hubs dedicated to precision fermentation in food production. Drawing inspiration from successful models such as Symbiosis Kalundborg (focused on pharma/enzymes), GreenLab Skive, the Illinois Biomanufacturing Hub (iFAB Tech Hub), Israel's Rehovot Biotech Hub, and The Singapore Food Agency's vision of achieving 30% food self-sufficiency by 2030—incorporating precision fermentation and cultured meat.

- Create large research test facilities and invest in process computational simulation

Economics of scale and high titer are the most important drivers to get down unit price. Companies at all stages should continue to prioritize strain development and optimize facility & equipment optimization.

Industrial scale precision fermentation of food ingrediens.



Soruce: BCG, 2024

Winning consumers

Consumers, being creatures of habit, are often reluctant to try new products, especially if the project do not meet functional requirement and fit into their lifestyle and routines.

Potential

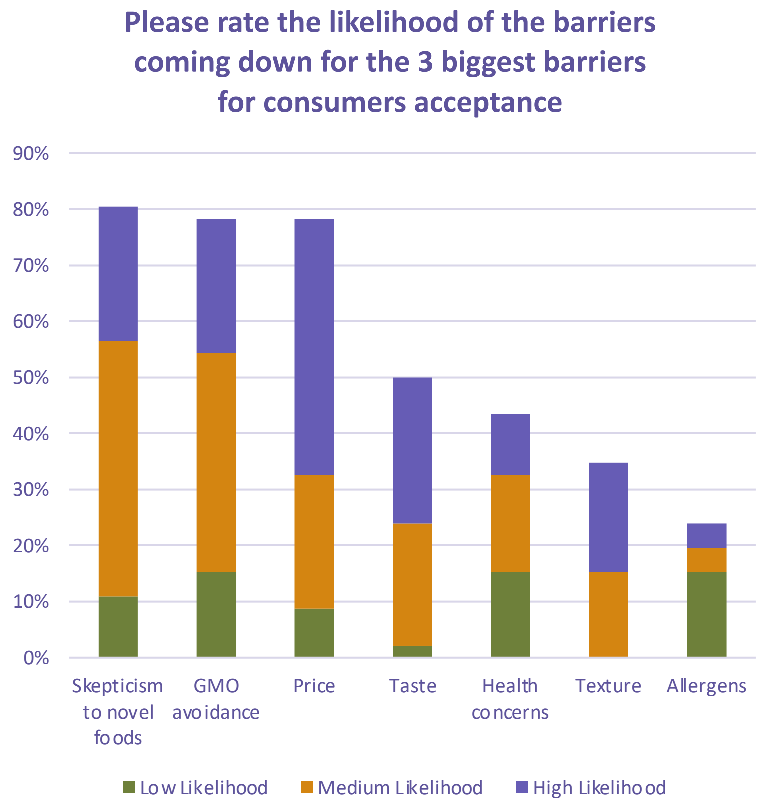
- The expert panel on precision fermentation identified three major barriers to consumer acceptance: "scepticism towards novel foods," "GMO avoidance," and "price." Over 75% of respondents agreed on these barriers being the primary barriers and exhibited confidence in overcoming them.
- A study by Aarhus University found that Danes generally exhibit openness to precision fermentation. To succeed in winning over consumers, products should emphasize sustainability and benefits. This can be achieved by disclosing carbon footprint, environmental impact statements in marketing materials, and displaying sustainability certifications. (Banovic, 2024)
- Consumers show preference for hybrid alternatives. Initial market introductions should combine conventional and animal-free proteins to meet indulgent and functional needs. This also serves to overcome initial negative taste perceptions.

Barriers:

- Consumer barriers include “Scepticism towards novel foods“, "GMO avoidance," and "price."
- Consumer are hesitant to pay for a premium for animal-free products.

Recommendations:

- Inform and create a dialog with consumers about precision fermentation of food.
- A British roadmap highlights the importance of consumer education and collaboration with non-profit organizations to instil consumer confidence(Innovate UK, 2022)



Source: CIFS Survey, 2024

Life Cycle Assessment (LCA)
for precision fermentation of food

The main driver behind precision fermentation of milk protein is climate mitigation. Currently the methodological choices in the life cycle assessment (e.g. allocation methods and system boundaries) as well as background data can have major impact on results. Lack of standardized methodologies and protocols for conducting LCAs can lead to inconsistencies in comparing results across different studies or products. Lack of reliable data in turn creates uncertainty as to the merit and benefits of precision fermentation with different numbers circulating, which may from impede action from investors and politicians alike.

Potentials:

- Having reliable data on mitigation potentials can help place precision fermentation as a key mitigating technology within agriculture, that cannot be ignored.

Barriers:

- Obtaining comprehensive and accurate data across all stages of a product's life cycle can be challenging. This includes data on raw material extraction, manufacturing processes, transportation, product use. The complexity of assessing environmental impacts across multiple life cycle stages can be daunting.
- Defining the scope and boundaries of an LCA can be complex, especially for products with multiple components or complex supply chains, which is the case with precision fermentation that could source different types of growth media depending on seasons.

Recommendations:

- Harmonized LCA guidelines for the industry is needed.

Source: Innovate UK, 2022: Alternative Proteins: Identifying UK priorities

Policy framework, incentives and tax

At current speed of emissions, the carbon budget that aligns with the 1,5 C scenario will be overshot in 5 years. There is an urgent need for decisive action on climate change. Regulations must target greenhouse gas emissions from livestock farming which already in 2030 must be reduced by 50% (Harwatt et al, 2024). By reducing dairy with 50% there will still be a room for daily fresh cow's milk products and gourmet cheese.

Potentials:

- Precision fermentation subsidies could redirect resources from overproduced agricultural goods towards more socially optimal uses such as the mitigation of climate change and if the potential social benefits of transitioning to precision fermentation outweigh subsidy costs, investment becomes justified.
- Precision fermentation is not competitive on its own and will not be developed sufficiently fast. Subsidies could be used as an instrument as has been the case with other renewable technologies such as wind power, solar and EV's to speed up market adoption.
- Externalities pricing or subsidizing precision fermentation can help address external costs associated with traditional food production, such as greenhouse gas emissions, nitrogen pollution, biodiversity loss, and natural beauty degradation, aligning market incentives with broader societal and environmental goals.

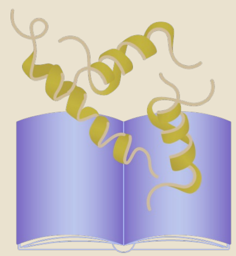
Barriers:

- Powerful lobby organizations that want to protect existing non-sustainable practices
- Lack of political ambition

Policy recommendations:

- Create an ambitious Danish and EU strategy that will foster investor confidence, this could involve EU Common Agricultural Policy declaring a peak livestock timeline
- Align agricultural subsidies with climate goals. Redirect subsidies from animal-based food towards alternative proteins.
- Stimulate commercial demand to underpin investments; for example, implementing market-pull regulations such as mandatory blending requirements, known from transport sector, such as the biofuels blending mandate.

"…livestock farming must be reduced in 2030 by 50%"



Danish production hubs scenario 2040

It takes 3-5 years to build an industrial scale precision fermentation plant with at price label estimated to DKK 2- 3 mia. Additionally, a hub ecosystem with all the service facilities it is estimated to amount something like DKK 10 mia. (BCG, 2024). Thus, it is important in due time to start long term infrastructure planning of the future hubs for precision fermentation produced milk proteins. To get an idea of need for skilled labor and the magnitude of infrastructure look to Kalundborg.

Potentials:

- These new hubs will drive industrial development of a whole region.
- Attract highly skilled employment and provide local tax payment
- Situate the new renewable energy hubs and fermentations infrastructure together – it could create synergy.

Barriers:

- There is a global race to attract investment in precision fermentation of food. However, investment, feedstock, energy, may jeopardize EU's ability to compete
- Renewable energy - bundant and cheap
- Water supply
- Growth media – locally produced
- Recycling of residual heat, bio-streams, water
- Logistic – transport hub
- Staff – qualified
- Capital – investment
- Ecosystem/supply chain for precision fermentation

Recommendations:

- Provide long term policy and regulatory framework at EU, Denmark, municipality levels to offer investor confidence.

Risks
Precision fermentation of milk protein

Risk and disruptions

Key to investing in promising new technologies is understanding the risk and barriers they face.

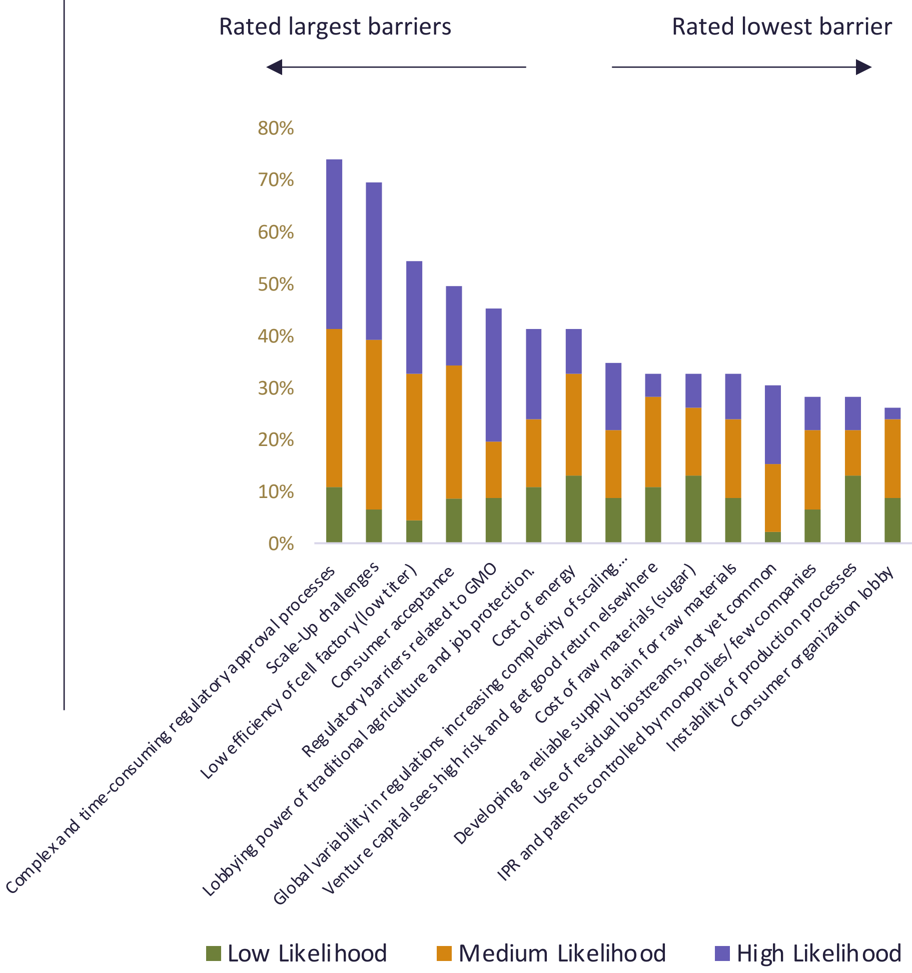
The survey of expert in precision fermentation reveals that the main barriers for precision fermentation production to become mainstream are EU Food regulations, scale up challenges, low efficiency (low titer) and consumer acceptance. Yet when asked to rate the likelihood of these barriers coming down, there is a confidence that the barriers won't continue to be barriers.

As part of creating the roadmap for precision fermentation of milk protein it is key to know what disruptive developments can sidetrack the industry. In this way these disrupters can be monitored for risk mitigations purposes and facilitate investors engagement and confidence.

The experts saw EU regulatory actions that could threaten precision fermentation as the key disruptive force - whether it be through costly and difficult EU approval procedures, a direct ban on GMO cell factory or job protection measures aimed at protecting existing dairy farms.

This means that a monitoring function could be put in place partly monitoring EU working groups and policies relevant to precision fermentation. Other areas to monitor could be the leading indicators of the economy and investment in green technology as well as public sentiment regarding GMO.

Risk to the precision fermentation industry



Source: CIFS, 2024

About the Roadmap

About

Network Animal Free Protein – fermentation produced milk proteins

The network is devoted to precision fermentation of milk protein. The Network gathers Danish competences at the crossroads of biotechnology and food production.

The network connects the resource base and bridges the gap between research, innovation, production, and the market. The network sheds light on opportunities and barriers in connection with production of milk proteins through precision fermentation.

The Network has created a pre-competitive forum across sciences, trade associations, businesses, consumers, and authorities. The network works throughout the value chain for recombinant milk proteins and aim to produce this "roadmap" building on Danish strongholds within food, precision fermentation and biotech.

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About
Roadmap
Paving the way towards animal free milk proteins

The roadmap is a joint publication of the project "Animal Free Protein - fermentation produced milk protein", ProteinFrontiers and Copenhagen Institutes for Futures Studies (CIFS). The Roadmap is a synthesis of: Thematic network meetings, study tour to Brussel, The Netherlands, and the "International conference on precision fermentation of milk proteins", January 22-23, 2024 Copenhagen, literature, newsletters and a survey done by CIFS.

Copenhagen Institute for Futures Studies

The Copenhagen Institute for Futures Studies (CIFS) was founded in 1969 by Professor Thorkil Kristensen, former Secretary-General of the OECD. It was set up in collaboration with a number of visionary organizations that wanted to qualify their basis for making strategic decisions through futures studies and foresight. Through research, analysis, seminars, lectures and reports CIFS identifies and assesses trends that affect the future nationally and internationally.

With more than five decades years of doing foresight, CIFS is an internationally recognized competence centre and one of the first of its kind specialized in foresight. CIFS' work is interdisciplinary. The staff represents different areas of academic and professional backgrounds such as economics, political science, ethnography, psychology, technology, etc. CIFS purpose is to help people and organisations imagine, work with, and shape their future.

COPENHAGEN INSTITUTE FOR FUTURES STUDIES

ProteinFrontiers

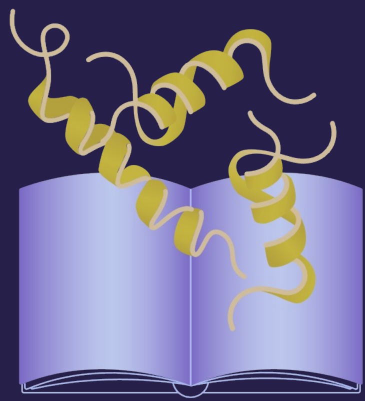
ProteinFrontiers is a startup food biotech company on a circular bio-economy mission to create new generations of sustainable, affordable, healthy, and tasty dairy proteins by precision fermentation using inexpensive production medias based on upcycled bio-residuals.

ProteinFrontiers is also the founder, facilitator and driver the "Network - Animal Free Protein - fermentation produced milk protein". Our vision is that Denmark shall be a leader in precision fermentation of milk proteins to phase out part of the dairy cows, reduce greenhouse gases, preserve jobs and create new export opportunities in the food sector.

The network has prepared this roadmap that describes potentials, barriers and recommendations for this to happen in Denmark.

ProteinFrontiers

Bibliography



Bibliography

Augère-Granier, M. L. (2018). The EU dairy sector: Main features, challenges and prospects. Available at: https://www.europarl.europa.eu/RegData/etudes/BRIE/2018/630345/EPRS_BRI(2018)630345_EN.pdf .

Banovic, M., Leardini, D., Grønhøj, A. & Aschemann-Witzel, J. (2024). Moo-Ving towards the Future: How to foster consumer acceptance of precision fermentation technology & animal-free dairy proteins?

Boston Consulting Group, 2021: Food for Thought - The Protein Transformation

Boston Consulting Group, 2024: Breaking the Cost Barrier in Biomanufacturing.

Carr L, Virmani MD, Rosa F, et al. Role of Human Milk Bioactives on Infants' Gut and Immune Health. Front Immunol 2021;12.

CIFS, 2024: Survey on the Future of precision fermentation of milk protein.

Good Food Institute (GFI), 2023: State of the Industry Report

Harwatt et al, 2024: Options for a Pariscompliant livestock sector.

Manifest and policy recommendations, 2024: How biosolutions can strengthen Europe's sustainability resilience and competitiveness: Manifest and policy recommendations. The European Biosolutions Coalition. 21 February 2024

Innovate UK, 2022: Alternative Proteins: Identifying UK priorities,

Marija Banovic, Klaus G. Grunert, 2023: Consumer acceptance of precision fermentation technology: A cross-cultural study. Innovative Food Science & Emerging Technologies,Vol 88,2023,https://doi.org/10.1016/j.ifset.2023.103435 .

Mazac, R., Meinilä, J., Korkalo, L. et al. Incorporation of novel foods in European diets can reduce global warming potential, water use and land use by over 80%. Nat Food 3, 286–293 (2022). https://doi.org/10.1038/s43016-022-00489-9

Milking the cap, 2002: How Europe's dairy regime is devastating livelihoods in the developing world (2002) Oxfam Policy & Practice. Available at: https://policy-practice.oxfam.org/resources/milking-the-cap-how-europes-dairy-regime-is-devastating-livelihoods-in-the-deve-114549/

OECD/FAO (2018), OECD-FAO Agricultural Outlook 2018-2027, OECD Publishing, Paris/FAO, Rome, https://doi.org/10.1787/agr_outlook-2018-en.

Tuomisto, 2024: Figure produced based on data from: Mazac, R.; Meinilä, J.; Korkalo, L.; Järviö, N.; Jalava, M.; Tuomisto, H.L. 2022. Incorporation of novel foods in European diets can reduce global warming potential, water and land use by over 80%. Nature Food (3) 286-293

United Nations Environment Programme (2023). What's Cooking? An assessment of the potential impacts of selected novel alternatives to conventional animal products. Nairobi. https://doi.org/10.59117/20.500.11822/44236

United Nations Environment Programme (2023). Emissions Gap Report 2023: Broken Record – Temperatures hit new highs, yet world fails to cut emissions (again). : https://www.unep.org/resources/emissions-gap-report-2023

Uutela, Rahikainen et all: Alternative proteins and EU food law, Food Control, Volume 130, 2021, https://doi.org/10.1016/j.foodcont.2021.108336.

Vegan Food Law, 2024, https://veganfoodlaw.com/

Xu, X., Sharma, P., Shu, S. et al. Global greenhouse gas emissions from animal-based foods are twice those of plant-based foods. Nat Food 2, 724–732 (2021). https://doi.org/10.1038/s43016-021-00358-x

Denmark needs to transform the food system to become climate neutral by 2045. It is a challenge but also a global business opportunity.

This roadmap outlines the necessary steps to develop a Danish precision fermentation industry for mass-producing milk protein.

The vision is to create a Danish hub connecting biotechnology and food production, opening new export opportunities for sustainable food ingredients. The roadmap hopefully inspire stakeholders and policymakers to shape the future food system reaching for sustainability, resilience, and carbon neutrality.

The roadmap addresses potentials, barriers, and recommendations associated with the value chain. It aligns with the overall ambitions of the green transition of the food and agricultural sectors to achieve the climate goals.

The Network Animal Free Protein – Fermentation Produced Milk Protein is supported by GUDP

Ministeriet for Fødevarer, Landbrug og Fiskeri

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