FLEISCHWIRTSCHAFT international 4_2021

How much longer will meat be made from animals? *Photo: Imago / Science Photo Library*

Global need for cell-cultured meat

Meat without animal suffering and environmental burden, but with taste and texture

The global meat industry is facing multiple challenges ranging from interrelated ethical, environmental, and business concerns. In the future, the words "meat" and "animal" will be decoupled. Meat without animals is the new notion of cellular biotechnology using stem cells and bioreactors as the basic platform to grow healthy and nutritious cultured meat.

By Henk Hoogenkamp

Human food consumption is projected to almost double by 2050 and demand is growing exponentially. Cultured meat products are an "and", not an "or" solution, and are the latest in a long history of optimizing food security. Meeting the world's protein needs will require contributions from large-scale production methods, including protein regeneration, all the way to small-scale animal farming. Cultured meat and seafood products will all play an important role in contributing to a balanced nutrition and environmental concerns.

The primary concern of the meat harvest traditionalists is that cultured meat does not involve raising and slaughtering animals. However, seen from a different perspective, cultured meat is an opportunity – not a threat – because it represents a new and better manner to provide much needed food for the global supply chain.

Global Challenges

Bioprocessing is the new way forward in the production of meat without intensive livestock farming. In the future, many high-value ingredients and products will be biomanufactured, including cell-free methodologies for developing more sustainable food for everyday life and overcome the limitations of conventional products that need significantly more water, energy, and land space. Hence, for companies to stay relevant, it will be essential to diversify outside of conventional product portfolios to assemble nutritious food products. These biomanufactured products should mimic the culinary, nutritional and technological profile of conventional meat, using precise and animal-free fermentation.

Growing meat without the use of animals is a rapidly emerging and highly innovative technology. The time has come to move past the need for conventional meat products and instead embrace new foods such as "plant-meat" and cell-cultured meat. The true benchmark for cultivated meat and seafood lies in a high production volume at a cost-efficient scale.

The Movers and shakers of change

The cultured protein industry continues to generate momentum. Currently, more than 80 start-ups are working on developing cultivated meat and seafood. It seems that multinational life-science companies, as well as the legacy food and meat processing industry, finally understand the potential of this emerging technology.

Even the world's largest legacy food company Nestlé has announced plans to enter this rapidly emerging industry. Singapore has become the first country to approve the commercialization of cultured meat and seafood. Local player Shiok Meats has introduced a cell-based crustacean and is also set to launch a cultured minced shrimp product in 2022.

Better and more

The development of human civilization was largely enabled by the domestication of livestock animals. In the future, cellular biotechnology is going to be the second accelerator not only in producing large quantities of cultured meat and seafood, but also as a resource for leather, silk, perfume, as well as vaccines and organs.

Conventional animal agriculture has almost reached its maximum capacity, and new technolo-

gies like cultured meat and bioengineered proteins are needed to lower the environmental impact. As the global meat demand continues to grow with approximately 2% each year, deforestation and the destruction of wildlife habitat are in the focus of public outcry. Especially the continuing deforestation of the Amazon rainforest for animal agriculture is an urging concern, while fresh-water sources are diverted from drought-prone regions. Smarter ways to produce food and meat for the daily diet are desperately needed to alleviate some of these pressures.

Cultured meat and seafood may hit competitive cost and environmental benchmarks by 2030. Initially, Asia, North America, and the EU countries are seen as strategically valuable markets to launch cell-based meat and seafood products.

Accelerated change

The use of animals as main food source can be seen as the main driver of catastrophic global collapse of biodiversity and thus responsible to irreversibly damaging the fragile ecosystem. By reducing livestock production, the rapid decay of atmospheric cattle methane emissions will effectively improve climate conditions. To reinvent the current food systems, it will therefore be essential to halt the collapse of biodiversity and slow-down climate change.

The controversy between meat consumption and climate change is heating up. The most heard arguments to eat less meat focus on the positive impact on the environment and human health conditions. Especially cattle and hog farmers are an easy target for anti-meat activists and are being subjected to one-sided criticism. Yet, most – if not all – western countries are under pressure to significantly reduce greenhouse gas emissions by 2025. Adhering to the EU targets, it will be necessary to tackle emissions head-on including the traditional agricultural methods. After all, agriculture is the second-largest emitter, following transport emissions, at approximately 14% of total emissions.

China calling the shots

When talking about meat consumption, something must be done, rather sooner than later. Take for example China: In the 1960s, the average Chinese person consumed less than 5 kg of meat annually. Fast forward, in 2020 meat consumption reached an astounding 63 kg per person. In 2022, China will be responsible for 28% of the world's overall demand for meat, and for 51% of pork products. Looking at these huge numbers, transformative protein selections will become important. "Plant meat" and "plant milk" are one of the choices, as well as cultured meat and seafood. These choices need to be made to reduce man-made greenhouse gases.

It will be crucial to improve biodiversity and boost alternative protein sources such as cultured meat and seafood, soy, corn, wheat, fava, and pea to meet the strict emission targets over the next decade. China's sign-off on carbon emissions will be essential for global reductions. If not, all other attempts will fail.

Cultured meat

The production of conventional meat in modern times is far from ideal. Livestock are routinely given antibiotics and hormones to accelerate their growth and muscle mass. Unsanitary outdated farming and slaughtering conditions may increase the risk of contamination from feces, as well as other bacteria and viruses. Unlike in factory-farmed meat, there is no use of contaminants and antibiotics in cultured meat products, therefore it is not contributing to antimicrobial resistance in human pathogens. Furthermore, it comes with many benefits for human health and environmental advantages, including "no-animal-to-food" conversion as well as huge savings on clean water and animal feed. Another major advantage of cultured food is that the manufacturing companies will only produce the parts of meat or seafood that consumers actually eat. In other words, they effectively reduce food waste, while providing year-round availability.

Cultured meat can be described in only four words: Cells > Scaffolds > Media > Bioreactors. In basic terms, cultured meat replicates conventionally produced meat through stem cell and tissue culture. Cultured meat will become a main disruptor of the current meat industry. It is poised to significantly expand humanity's capacity to feed a growing global population, while not only preserving the culinary traditions and preferences, but also protecting the planet. By its very nature, cultured meat will reduce the need to breed, raise, and slaughter animals. It should also be said that approximately 99% of all animals used for food are intensively bred and "farmed". Hence, these products can be considered as industrially grown and harvested.

Biomedical expertise

The ongoing challenges include finding better cell lines and nutrient media to feed those cells, scaffolding systems to shape the cells into tissue meat, as well as building bioreactors for large-scale production of meat that is eco-friendly and ethically sound.

Cultured meat development is complex. It crosses many scientific and technological disciplines such as biomedical applications and hardware engineering, which, when combined, will ultimately create a new field of scientific expertise. Scaffolds need to be designed to enable the growth of different types of animal cells imitating intramuscular fat as well as connective tissue.

Scaffolds provide a support structure for cellular adherence and various component cells of the integral meat composition. They can be seen as netting (e.g., made from soy protein), which allows the cells to multiply and intertwine until a certain predetermined shape has been formed. Then, there are also developments to create plant-based microcarriers that will enable tiny particles to which the cells attach while suspended in the media. Some cultured meat companies use scaffolding systems called electrode spinning: a three-dimensional nanofiber scaffold used for regenerative medicine and tissue engineering. This technology transforms different synthetic or organic compounds into a structural replacement for the non-muscle, non-fat (extracellular) protein in all types of cultured meat, including factoring in variables such as vitamins, minerals, and growth factors.

Meat biomanufacturing

Technological advancement now makes it possible to cultivate meat without animal serum. For example, bovine identical serum can be synthesized. Cells can now be cultivated in bioreactors using animal-component-free growth media. For example, removing Fetal Bovine Serum (FBS) from the growth medium is a great step forward in bringing down the production costs and ultimately helping achieve price parity with conventional animal-raised meat. The latter is especially true for beef.

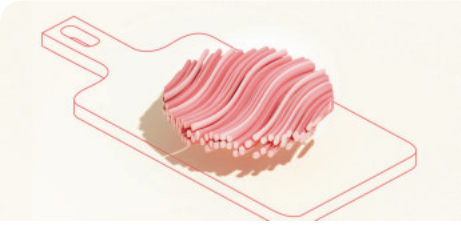
Mosa Meat (Netherlands) and Upside Foods (USA), as well as other start-ups have made major process improvements by significantly reducing the cost of the growth medium to enable large output quantities of cultured meat. Specifically, the removal of Fetal Bovine Serum: a substance, which is not only expensive, but also ethically and morally controversial because it is taken from the blood of pregnant dairy cows during slaughter.

Growth media

The key growth medium ingredients are salts, sugars, and proteins. An often-neglected part in many publications and articles on cultured meat and seafood is the importance of buffer and trace elements as essential nutrients. Nutritious miner-

A 0.5 g sample taken can lead to 80,000 burgers from one sample. *Illustrations: Mosa Meat*

The process consists of replicating the natural environment where the cells are multiplying into trillions. It is important that the environment is oxygen-rich and temperature controlled.



The advantage of muscle cells: they merge naturally. Fibres from one sample, placed in a gel that is 99% water, can grow to 800 mill. strands of tissue.

After reaching maturity, the muscle and fat components are combined and prepared for cooking.

als for upstream and functional salts for downstream processes are needed to secure the biotechnological performance. These bioprocessing salts need high solubility and the absence or at least low levels of heavy metals and endotoxins. As the cultured meat and seafood industry is maturing into a self-supporting business model, specially blended functional salt premixes will be made commercially available, including certified Kosher and Halal mixes.

The protein components are made from recombinant microbial systems, expressing proteins in microbes such as fungus, yeasts, and bacteria. Stabilizing the cell lines and cultivation in suspension, while optimizing the proliferation or speed of multiplying, are all important processing steps.

Growing inexpensively

Cell-cultured media is the most expensive step of the cultivation process and lowering the costs of the base media will immediately translate to refining sustainability, as well as to lower costs across the value chain. The basal media is made up of the nutrients that the cells absorb as they grow or components that trigger the growth of the cells. The ideal combination is using water, or by-products from the food and feed industry that have a low carbon footprint. Lowering basal media costs can also be accomplished when pharma-grade ingredients are replaced with food-grade components.

Fat is key

Fat is where much of the distinctive flavor of meat resides. In addition, meat flavor also comes from the breakdown of collagen. Therefore, it will be necessary to cultivate different types of cells to truly simulate the desired meat flavor profiles. Cultured fat – under development by a.o. Mosa Meat, Perfect Day Foods, and Cubiq – is made using different types of fat starting from stem cells without the use of GMO material. These companies are known for their creation of clean fats by using cell-culture systems. It can be argued that the inclusion of cultured fat will be cost prohibitive, especially in products that traditionally contain high fat levels such as a beef burger. Burgers typically have approximately 20% fat, a level probably too high for cultured beef fat, even though the flavor attributes improve considerably. Subsequently, it is likely that at much smaller inclusion levels, the cultured beef fat can be infused with natural spices and flavors. Flavor companies are expected to develop a range of "flavor-infused" cultured fat products.

3D cellular agriculture technology

Muscle meat is probably the most complex food that exists. Not only in its raw form, but certainly its transformation during cooking, creating complex sensory parameters delivering much-preferred culinary experiences. As for cultured meat, it is far more difficult to create a perfect whole-muscle beef steak than a simple finely ground hamburger. 3D bio-printing for cultured meat can provide unique solutions to key problems, especially adjusting protein cells, fat, and other nutrient components, as well as providing the desired organoleptic properties. Crucial in creating a cultured steak is the use of multi-material 3D printing technology allowing different meat fibers, connective tissues and fat cells to be layered in one single process. This technology needs to fully replicate texture and mouthfeel for cuts such as sirloin and rib-eye steaks.

A 3D replica of a conventional beef steak or salmon loin is now within reach for cell-cultured products. Not only replicating the appearance, cutting properties and nutritional value but also duplicating sensory qualities such as flavor and texture.

For 3D printed products the challenge is to create the right nutrients and combinations that allow the multicellular matrix to simulate conventional muscle structure. The tools needed are a strong bio-engineering platform, an animal-free growth medium to nourish the cells and bioreactors to grow the tissue. Many of these tools have been previously developed by the medical world using bio-tissue engineering and the help of scaffolds for medical organ transplantation.

It looks like 3D manufacturing technology called stereolithography will be a possible contender to create a specific structure of muscle and fat marbling and texture of a "real" structured beef steak. 3D printing is well on its way to become the choice for prototyping or a structured endeavor, enabling rapid development at significantly less cost.

3D technology has now entered the cultured or clean meat vocabulary and it specifically allows the combination of all cells that make up conventional meat simultaneously, such as muscle fibers, fat cells, blood vessels, and connective tissues (collagen).

Regulatory hurdles

Even though both Singapore and Israel have already given regulatory approval for the consumption of cell-based meat and seafood, the industry still faces major challenges in regulatory approval in the US and the EU. The U.S. Food & Drug Administration (FDA) will mainly oversee the procurement of cell-collecting systems and cell-culturing technology, while the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture (USDA) will be responsible for processing and labeling the products from the harvested cell-based meat products.

A major and still unresolved challenge facing the cultured meat industry in most countries, is the lack of governmental regulative framework. Except for Singapore, Qatar, and Israel, no jurisdiction has yet approved cultured meat to be released for human consumption. This is mainly because legislative approval will likely be slowed down by the lack of detailed safety data from large-scale consumer consumption studies, as well as the opposition from the conventional meat industry and farmers. Proactive regulatory action is needed now that cultured meat is nearing market introduction in the US and the EU. A clarifying regulatory pathway needs to be agreed upon between the USDA-FSIS and the FDA, as

Mosameats goal is a burger that's just like a regular burger.

well as rulemaking by the European Food Safety Authority (EFSA).

Labeling vs. name calling

Although in the early days of "alt-meat" many name suggestions where used in articles and publications, it is likely that within the USDA there is now consensus to choose either "cell-based meat" or "cultured meat" as the name of choice for consumer identification and recognition. The main rationale to choose one of these names is that the cultivated meat is made in a bioreactor. These names also help most consumers to understand that the new food products are produced in a different way from conventional meat .

The EU landscape, unfortunately, is quite different from the US. Europe is rather conservative and cell cultivation ruling will need to be approved by EFSA, which in practical terms will likely be a major handicap to get these innovative foods to market quickly. Most likely, China and Japan will have regulatory approval for cultivated meat before the EU does.

It is not an easy task for government regulators to adequately differentiate cell-cultured products from the conventional meat products. There are opposing views between the animal farming community and the cell-cultured disruptors. It is no surprise that animal farmers prefer keeping the monopoly of using the word "meat" so as not to confuse consumers with emerging biotechnological methods of assembling or growing a group of cells together in a bioreactor.

It will also be important to communicate via label if growth-enhancing "additives" are used when producing cell-cultured foods. The consumer has the right to know, so that informed purchasing decisions can be made based on the presence or absence of various support or processing additives in cultured products. Whatever the regulatory outcome, it is important to acknowledge that scientific innovation and progress should not be stymied. If cultured meat products are equivalent to their non-biotechnological counterparts, the new wave of food disruptors should not be required to encounter any further regulatory hurdles.

The marketing dilemma

Sustainable food supply is a defining issue of the 21st Century, and the main reason why there currently is an emergence of alternative protein sources creating innovative technologies to guarantee food safety for a rapidly growing world population.

As frequently proven in the past, consumers are usually hesitant to embrace new technologies, which is also true for food products that are still on the drawing board. Most consumers have difficulty envisioning these products when they are not physically able to see and try them. Consumers are usually notoriously skeptical of food tinkering, especially when it is called "biotechnology". For cultured meat companies, it is therefore a smart marketing strategy to slowly and carefully introduce their products to the market. Smart public relation efforts are key to engage the eco-conscious consumer and share the advantages of meat products which have always been deeply embedded in religion, socio-culture, and culinary enjoyment.

The demand for a more sustainable food system is truly global and rapidly growing, with much of the shift being led by the sub-30 age generation. However, when the new product that looks and tastes great, becomes commercially viable, consumers are likely to switch from old to new and start enjoying meat products that can now be eaten without the negative impact on animal welfare and the environment.

Initially, cultured meat will cater to those consumers who prefer the texture and taste of conventional meat but do not want to cause animal suffering and environmental damage. Specifically the younger generations will be seen as the real decision-makers on whether cell agriculture is going to be a successful part of the global food industry. Already, in a few countries, cultured meat is available to affluent consumers in selected restaurants. However, cultured meat ultimately needs to achieve societal benefits not just fort the happy few, but for the entire global population.

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