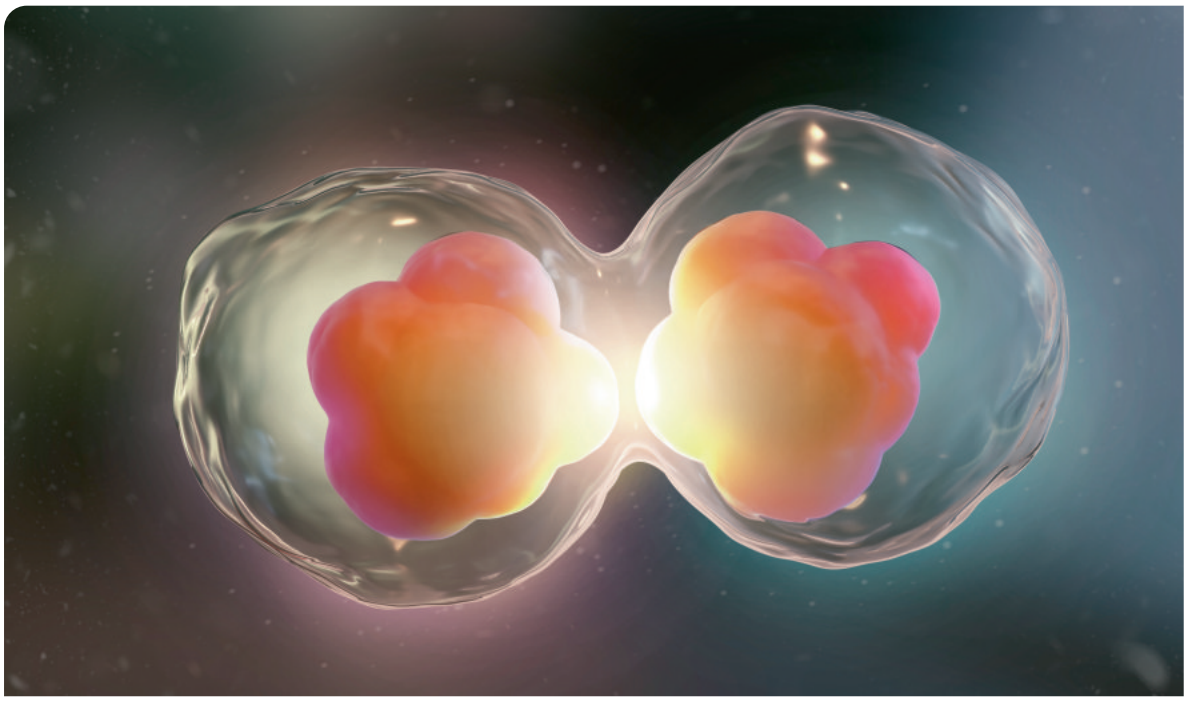


One of the smallest parts of animal bodies, stem cells offer the most potential for developing lab meat. *Photo: Adobe Stock / Anusom*

# In the cell lies the power

## Cellular agriculture on the rise – Biology from the laboratory will replace familiar structures

**The concept of laboratory meat is constantly evolving in cellular agriculture. Changes are imminent, the consequences of which are difficult to estimate. The field of biotechnology in particular is triumphant – biology from the laboratory will replace familiar structures. Is a cellular revolution imminent?**

**By Henk Hoogenkamp**

The future of bio-organism engineering is software and hardware automation. In other words, biology by design will replace much of the legacy technology by self-replicating and self-repairing renewable molecular structures that build cultured ingredients or products via fermentation with engineered or modulated yeasts or fungus support. Designer enzymes are an integral part of these bio-industrial applications, ranging from cheese-making to pharmaceuticals, or from textile fabrics to ecologically friendly cleaning agents.

Biotechnology is a uniquely powerful technology that can reduce or eliminate the need to grow and manufacture everything. Instead, DNA modification is the new platform which can create amino acids (the building blocks of protein). Relatively speaking, cellular biotechnology today is still at its very early stage of success.

For the food industry, biotechnology has the potential for reducing demand for cattle and meat-producing animals, even as the demand for dairy and meat rises. Cultured milk protein and cultured meat can probably be seen as one of the biggest technological leaps for humanity by using up to 90% less land, water, and greenhouse gas emissions rather than conventional dairy and meat production.

### Reshape food for future generations

Agricultural civilization came before the technology-driven era by several millennia, but technology-driven inventions have since overpowered agricultural domination. Cellular agriculture has less negative ecological and environmental footprints or side effects compared to traditional farming and intensive animal production for human consumption. Cellular agriculture is a true groundbreaking entrepreneurial field, some of which are still in its early conceptual phase and in need of additional funding.

Whether explicitly or implicitly, the United Nations Sustainable Developing Goals to turn around world's fortunes by the year 2030, have a strong relation to food. The collective food industry is grappling with the question of how to ensure sufficient nutritious and tasty food for the burgeoning global population, while at the same time reducing reliance on fossil fuels, maintain clean-water status, improve biodiversity and reduce greenhouse gas (GHG) emissions.

At a closer look, one can say that the animal agriculture sector is the single largest anthropogenic user of land, contributing to reduction of fresh water supplies, soil degradation, and air pollution. To relentlessly increase food production, valuable rainforest is often forcefully converted into farmland and this form of deforestation leads to loss of biodiversity of the most precious natural resources. Yet, with the world population rapidly growing to about 10 billion by 2050, the current food production needs to increase by approximately 50 to 70%, while only some 5% extra agricultural land is available.

The environmental challenges facing the global agricultural industry are increasing. Alternative and smarter ways to produce foods for the dietary requirements will alleviate some of these pressures. However, as new cellular agriculture technologies continue to emerge and are nearing commercial introduction, a one-size-fits-all implementation and legislative approach may not probably work.

The world's future is the (r) evolution of society where animal products are animal-free. In a broader sense, biotechnology is the interface between biology and engineering. "Silicon Valley in-

vestors" are attracted to synthetic biotechnology and synthesizing whole genes or genomes, which are now becoming more like the disruptive value propositions that will define technology-driven business models in the future.

## Building life from scratch

Biotechnology and bioprocessing focus on the wide range of methods used for transformations like yeasts, enzymes, bacteria, as well as other fungi, plants, and plant cell cultures. These food and agricultural products are described as "green biotechnology".

Biosynthesized technologies will propel the development of sustainable protein cultured through microorganisms. Fungi-induced "brewing" or fermentation offers an excellent nutritional profile, including an amino acid composition similar to animal protein sources like meat, dairy, and eggs.

Fast forward, the possibility of producing proteins from local crops such as cassava, beets, and sugar cane is a main incentive to meet environmentally sustainable proteins that also reduce expensive protein imports in developing or poor countries. Finally, these countries can become self-reliant in their protein needs. Just think about the colossal currency savings if the production of animal-free milk proteins and cell-cultured meat can be done locally by developing countries.

Biosynthesized proteins are still in the experimental stage and expected to reach commercial use in 2022. A few biosynthesized proteins are already commercially available in the US and cleared by the FDA, though in the EU are still subject to regulatory approval such as EFSA Novel Food requirements.

Capital venture investors see DNA modification as the next programmable venture with massive opportunities for the collective food industry, medicine, and biopharmaceuticals, including potent painkillers and cancer medication. The speed of innovation is at times difficult to grasp, but it is evident that the accelerating transformation of the global food system is caused by truly innovative and scientifically driven technologies, combined with improved marketing that will create sustainable and nutritious foods.

Quite a few of these capital venture companies see biotechnology as a scalable innovation with a decent capital to growth ratio, not to mention that having cultured meat, medicine and food security is a good environment to be in.

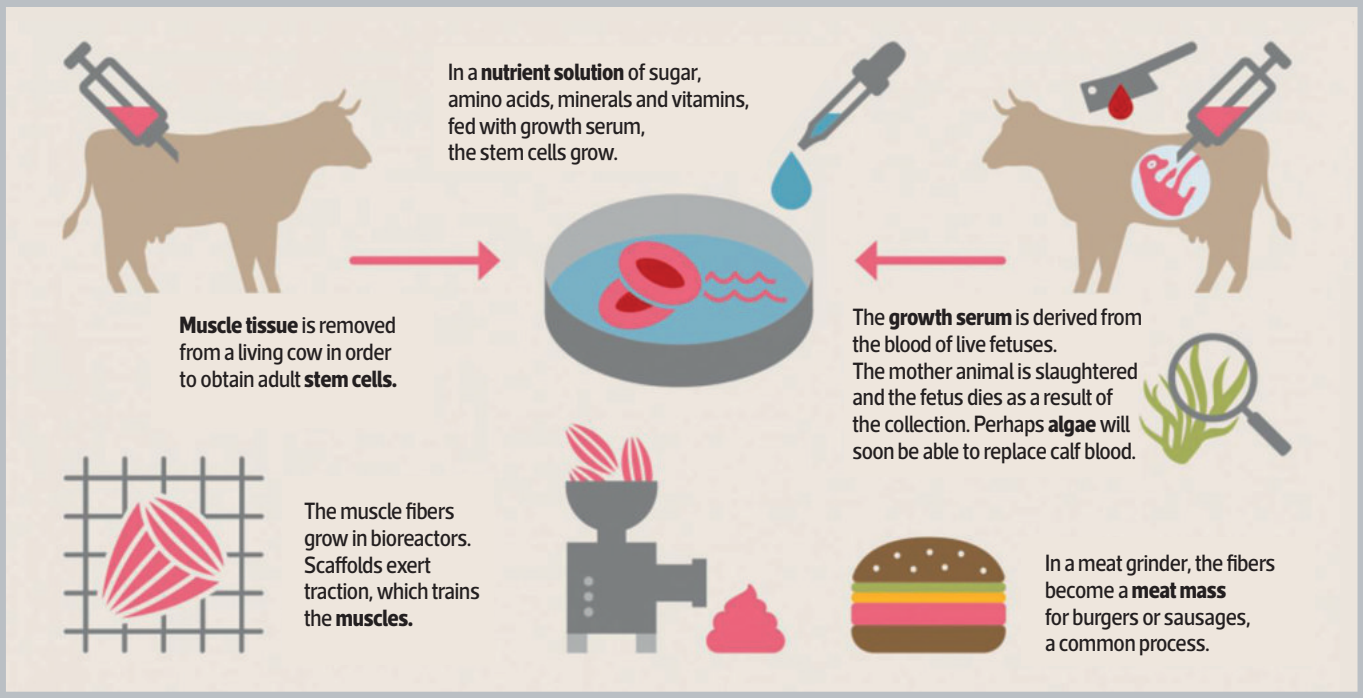
The huge increase in anticipated food production cannot rely on the traditional or conventional farming practices alone. A fundamental shift in thinking will be needed with the acceptance of new protein sources such as those grown without using valuable land but instead created from cellular biotechnology, including heterological protein expression and even single-cell organisms -specifically called hydrogenotrophs, that act like plants in converting carbon dioxide ($CO_2$) into food. Bacteria assimilate $CO_2$ directly as a carbon source and will be the first bacterial protein product meant for human consumption.

Carbon transformation technologies are not only suitable for food production, but also ideal for conversion of carbon-based materials into biodegradable polymers, as well as conversion of carbon from the air into biostimulants for depleted agricultural soil. In the meantime, more start-up companies are developing unique proprietary processes and are well on their way to enter these potentially lucrative market spaces. Regenerative agriculture will become one of the ways forward to capture the need for more food of higher nutritional quality.

## A disruptive force

The science of tissue engineering – like growing functional organs for people – is similar to growing or cell-culturing muscle meat or fish

## Process illustration




Source: Fleischatlas 2018 / Vier Pfoten, Stockmar FLEISCHWIRTSCHAFT international 3_2021

A simplified illustration of how in vitro meat is produced - so perhaps the burger from the Petri dish will soon be on consumers' plates?

tissue. Perhaps the only difference is scale and magnitude of production. It certainly is no coincidence that medical professors and doctors started entrepreneurial cellular biotechnology food companies and now have become the poster child of cellular agriculture.

Tissue engineering is a relatively new science mostly generated from chronic shortage of human donor organs or tissues for transplantation, a gap that may be filled using re-engineered organs such as skin, cartilage, and other soft tissues like muscle. These applications need to perform and maintain a biological function as they are used in a living person without being rejected.

The technology of regenerated biological material for medical applications is strikingly similar to the one used for the creation of, for example, cultured meat. Actually, the only difference is that synthesized cell-cultured meat needs to duplicate or simulate organoleptic quality such as color, taste, and texture, as well as be similar nutritionally. Examples are companies like Mosa Meat, Just Meat, and Upside Foods.

Cellular agriculture and post-animal cell culturing are emerging together with new technologies like 3D printing, regeneration of human tissue, artificial intelligence, QR (quick response) codes, augmented reality, virtual reality, and robotic interfaces. The use of 3D printing to create highly personalized nutrition is now within reach of commercial introduction. This technology can be applied to both the plant-based and cell-cultured meat sectors, providing nutrient-dense food options not only for those on special diets, but also throughout the entire food supply chain.

Meat in the form of muscle appearance is probably the most complex food product that exists. Not only in its raw form, but certainly also its transition during cooking, creating complex sensorial parameters delivering much-preferred eating experiences. As for cultured meat, it is far more difficult to create a perfect whole-muscle beef steak, than a simple finely ground hamburger. Crucial to creating a cultured steak is the use of multi-material 3D printing technology allowing multiple different meat and fat cells to be layered in one single simultaneous process. This technology uniquely allows to fully replicate appearance, texture and juiciness for cuts such as sirloin and rib-eye steaks. 3D printing is well on its way to become the choice for prototyping or a structured endeavor, enabling unprecedented fast development time at significantly less costs.

### Software and hardware automation

Recombinant DNA technology used in expressing genes in microorganisms (which are normally not expressed) to produce proteins can augment armamentarium to battle food security issues. However, the very same technology can also be used to create new industrial materials, most of which are not even on the radar screen today.

With the help of artificial intelligence (AI) and software directed robots, a few scientists can now equal or surpass the output of numerous traditional scientists and technologists working bench top in a much shorter period of time.

Presently, one of the biggest challenges facing the synthetic biotechnology upstarts is the issue of transparency. This has been the center of debate around genetically modified organisms or GMO. It is clear that cellular agriculture is ahead of government food regulatory guidelines with looming issues that need to be addressed, such as labeling and safety.

Using biotechnology and bioengineering as manufacturing tools is the most sustainable option to move forward, and the possible use of GMOs should not be hidden from the public. To safeguard the future of the planet, synthetic biotechnology will be essential to sustain life and wellbeing for the human race. “We should not try to run before we can walk” – ergo every measure should be taken to prevent the mixing of GM organisms with the natural world until the impact is fully understood.

### Artificial Intelligence (AI)

Technological disruptive food innovation and strategies are needed in order to successfully link existing and emerging know-how such as cellular (synthetic) biotechnology, human health, artificial intelligence (AI), as well as new business models. Artificial Intelligence (AI) will be shaping the future of the food and beverage industry. AI will not only predict yields and production processes

and efficiency, but also enable ground-breaking innovation with unique developments of food ingredients such as superior flavorings and colloid stabilizing systems.

Nevertheless, we need to pause for a moment and realize that progress seldom follows a linear line. This will certainly cause hick-ups with automation, robotics and artificial intelligence predicting to destroy employment in developed countries. Most threatened are the low-skilled workers, many of whom currently serve as the backbone of the economy. It will not stop there. Reports say that artificial intelligence can better diagnose diseases than doctors like radiologists and dermatologists, thus triggering questions about algorithms taking over a great part of the medical industry.

The bottom line is to answer the variables of technological unemployment - the gap between jobs created and the jobs killed after yet another disruptive invention. In a rather unique way, it is becoming evident that disruptive technology may not only kill jobs but also exacerbate inequality as profits go to a far smaller portion of society. These issues need to be discussed because equal representation and sharing remain the backbone of a healthy civilization.

## Entrepreneurial thinking or staying put?

Science and technology are the sources of innovation, whereas entrepreneurial thinking with strong leadership, coupled with strong disciplinary and organizational structures, usually create the competitive edge. For some legacy food companies, experience and expertise often become a barrier to success and hinder progress, which are usually driven by singular "even-keel" or risk-free thinking void of disruptive creativity.

These changes are obviously fueling anxiety among legacy food companies like Nestle, Unilever, General Mills, Pepsi Co, Coca Cola, Kraft Heinz, Kellogg's, and Friesland Campina, many of which wonder how much disruption they can tolerate and how much they should embrace. The answer is often a balancing act: it is good to look at the future, as long as it does not disrupt the shareholder and still presents stakeholder values. For many legacy food companies, it is clear that change can be painful for the organizational structure, particularly when business is going well. Moreover, legacy food companies tend to have a culture of risk aversion and opt for zero-risk tolerance when thinking outside the box.

## Post-animal food going forward

Throughout history, people have selected animals, plants, and microorganisms to enrich the wholesomeness of the food supply by intentionally crossbreeding to improve hereditary makeup. From this perspective, there is nothing new about cellular and gene technology.

Biotechnology is presently in the Stone Age, comparatively speaking. Its application to food production has only scratched the surface. Biotechnology, particularly cellular agriculture, will eventually utilize renewable energy sources and address consumer needs with wholesome food and other daily products, as well as provide the world's rapidly growing population with ecological sustainability. The technology – also termed post-agriculture food production- has the potential to create cleaner, cheaper, and more flexible food production

Pea protein is one of the most widely used bases for meat alternatives and has a much better reputation than soy-based alternatives, for example.

A flavored coconut-based beef fat alternative can be used for use in plant-based burgers. This improves flavor and prevents shrinkage during preparation.

Burgers are one of the most popular plant-based products that are now available to eat and buy almost everywhere – for example, even on a flight with KLM.

methods, while leaving fewer "fingerprints" in the areas of waste, animal health support, and supply chain management.

Cellular agriculture is a true groundbreaking entrepreneurial field that is still in its early conceptual phase and some start-ups are in need of additional funding.

History has shown that people are skeptical or even hostile when confronted with breakthrough technologies, especially when it comes to food. For example, early in the introduction of genetically modified organisms (GMOs), American companies raised false and misleading expectations, as well as made predictions that were self-beneficial and self-centered. As a result, consumers were confused by the extreme complexity of the issue.

Although cellular agriculture is not directly linked to the GMO controversy, its clean and pure technology should be communicated through an open and honest dialogue with all stakeholders.

## Facilitated expression

Scientists are only scratching the surface when it comes to unlocking the potential of precision or microbial fermentation to produce food ingredients. The application of biotechnology to food production is only the beginning of a long road to ensure future food security and safety. For an increasing number of food products, microorganisms are the future of nutrition.

A primary advantage of cellular bio-factory manufacturing is the lack of waste streams at the end of the fermentation process. Once the fermentation (using sugars and other low-cost biomass ingredients) has been completed, the individual components can be mechanically separated, if needed. This technology – also known as "facilitated expression"– can be used with or without genetic engineering.

Throughout history, people have selected animals, plants, and microorganisms to enrich the wholesomeness of the food supply by intentionally crossbreeding to improve hereditary makeup. Seen from this perspective, there is really nothing new about cellular and gene technology. From another perspective, it has become apparent that protecting biodiversity is paramount and we have to accept the reality that man has already made an irreversible impact on the natural world. Until our disruptive technologies are better understood, it is imperative to find a socio-technological equipoise position that allows forward momentum while simultaneously filtering out the poisonous legacy of the global industry lobby.

## Digital genetic coding

In essence, proteins can be so much more than just food: proteins are highly customizable providing a huge range of functionality for product development. Designing and synthesizing original proteins can create an endless range with unprecedented versatility.

Recombinant proteins can help solve the food security issues all the way towards creating new industrial materials, most of which are not even on the radar screen today. With the help of artificial intelligence like software-directed robots, biosynthetic technology is the next wave of manufacturing by using digital genetic coding, giving it the ability to scale like a software company.

An increasing number of people worry about what happens when artificial intelligence renders their expertise obsolete. Not only the taxi drivers will lose their job to autonomous-driven cars, but also the medical doctors like radiologists and dermatologists may see their jobs conceptually change or even disappear.

What will artificial intelligence (AI) mean for income-generating jobs and its impact to society? Silicon Valley's autonomous cars developed by Tesla, Google, and Apple could turn Detroit's legacy auto manufacturers into low-margin assembly lines making chassis to carry around computer electronics of technology that is not owned. For now, it looks as if the self-driving car technology will be ready before people are ready to give up command of the wheel.

## Radically altered landscape

In general, the rather traditional food industry is bracing for rapid technological change that can radically alter the landscape. As a matter of fact, the technological changes are happening so rapidly for it to be predictable 20 years from now.

Advancements in artificial intelligence (AI) have broad applications in the agricultural and food processing industries and these innovative technologies will improve multi-disciplinary sectors such as bioinformatics, molecular bioscience, crop improvements, animal welfare and robotics, including intuitive human-robot interactions.

The disruptive presence of quickly-advancing cellular biotechnology start-ups is being felt and is shaking up conventional research structures, which are now in need of recalibrating human talent interactions toward the skills from digital and artificial intelligence.

## The only constant is change

In the US, the existing regulatory framework of biotech products dates back to 1986 and has since remained largely untouched. The huge innovations in biotechnology -like human tissue engineering and many forms of cellular agriculture- urgently need to be updated from a regulatory perspective with joint input from Government authorities, such as the FDA, USDA, EPA, EFSA, and biotech's greatest minds.

The world of food science is quickly marching into new territories using post-animal biotechnology and bio-economy models to provide sustainable and healthy food security and nourishment for a rapidly growing world population.

Newly designed protein molecules can balance performance and productivity and are a necessary tool to reduce go-to-market costs. This is accomplished through a bioinformatics analysis of amino acid sequences and genetic codes to achieve and master variables like elasticity, tensile strengths, and heat tolerance, subsequently providing a unique revolutionary platform for the creation of innovative and sustainable, as well as high-performance products.

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