



ILSI 2021 Annual Symposium Session 6: Alternative Proteins

Transcript of the presentation, **Scalable Technologies for the Production of Alternative Proteins: A Review**, [Blake Byrne](#), The Good Food Institute, United States

Really pleased to be here, and in as few words as possible, what we'll be discussing today is a look at alternative proteins. And alternative proteins as GFI terms it is really the use of plants, the use of microbes, or microbial cells via fermentation, and the use of animal cells and animal cell culture, to create products that are conventionally produced via animals.

So, in the purposes, or for the purposes of this talk, we'll primarily be focusing on production of meat via these alternative platforms. And really what I want us to home in on here is their potential for scalability, as well as the pricing potential of these products. It is GFI's thesis that in order for alternative proteins to really take off in this industry, they have to taste the same or better, but ultimately, they have to cost the same or less as commoditized meat, egg and dairy products.

But I'll plant the flag here and just start by telling you all a little bit about GFI, some of you all may be familiar and others certainly not. And so GFI is an early donor funded nonprofit, we really exist to advance both the markets and the technology of alternatives to conventional animal products. And so, we do so not only in the United States and in the EU, but also throughout Brazil, in Israel and India, and throughout the Asia-Pacific as well. We have about a hundred plus staff in these regions and really focus our efforts on three key programmatic areas, if you will.

The first is science and technology, the team that I am on, and the science and technology team really focuses on advancing the open access foundation for the alternative protein industry. And ensuring that we're creating basically a sound foundation of science, and a pipeline of scientific talent to essentially serve as the next generation of science and technology in alternate proteins.

Our corporate engagement team. This team really focuses on working with the largest food and meat companies in the world, all the way down to just an entrepreneur with an idea and helping companies and owners craft theses around alternative proteins. And in the cases of large companies, actually developing strategies to help them transition their supply chains, from say, conventional meat production, to alternative protein production.

And then finally our policy team. So, our policy team works in not only efforts to create a fair playing ground for alternative protein products, both again in the US and elsewhere, but also advocating for an infusion of public sector funding into alternate proteins. Really seeking to establish alternative proteins on a level playing field with clean energy as an actual solution for a green economy, and for mitigation of things like climate change.

So, I'll transition us now a little bit to a framing which I think a lot about in my time at GFI, and it's the concept of total meat. And this idea, of course, it's really the idea today in... excuse me, globally. We produce in the neighborhood of 350 million metric tons of meat via conventional means in animal husbandry every single year. And of course, by 2050, in the next 20 to 30 years, that demand, and ultimately that production, is expected to increase by nearly 50%, to 500 million metric tons of meat production in a single year, to satisfy growing meat demand.

Now, of course you can see in the top left of the screen that alternative meats, meat from plants, meat from microbes, and meat from animal cell culture, these products are really a rounding error of the overall global meat market. And as it stands today, this massive earth system that we have, conventional animal agriculture produces a vast volume of meat, which in many ways is cheap and affordable, and it tastes good. That's a reason why it is the predominant system.

But of course, as many of us know, this system that we've created that does quite a good job in the context of providing cheap and delicious protein, also has really disproportionate externalities on our planet. So, I won't belabor you all with the details of the issues with conventional animal agriculture, aside from saying, conventional animal agriculture, as we know, is a significant contributor to global greenhouse gas emissions. It is a massive utilization of our total global arable land mass. And it is fundamentally a system that relies on the efficiency of feeding crops through animals to create protein, albeit delicious protein.

And then finally, there are significant public health concerns when it comes to conventional animal agriculture, which again, many of you are familiar with. And again, this is essentially just a parcel of the system which we've created. Today we use in the neighborhood of two thirds and three quarters of all antibiotics globally for animal husbandry, industrialized animal agriculture. And if you ask the WHO, they will say that this utilization of antibiotics in agriculture, and in animal agriculture, is a significant threat, not only to human health, but to global human health.

And so, we think that there are ways in which of course we can produce meat while eliminating some of these really onerous externalities. So, at GFI, our organizing question, and what I go into my day with every single day, is how do we get to this state of the world? Where we're really producing some, most, or even all of our meat by 2050 via these alternative protein production platforms. And of course, as I've referenced here, the three production platforms, which I'm going to go into detail with more on the technical side of things here in a moment, are plant-based meats, they're fermentation powered proteins, and then cultivated meat as well.

So, in all of this, as I referenced... That can slide by. Ultimately, our theory of change, if you will, is that for these three production categories, the only way that they emerge from an obscure, small segment of the market, this niche play, to being viable, scalable, industrial alternatives to conventional meat, is if we optimize these production platforms for price, and if we optimize them for taste. These products have to taste the same or better, and they have to cost the same or less than conventional meat products.

Now, once we do that, it is our belief that you take out all of the other considerations around animal welfare, around environmental calculations, public health. All of the things maybe that some of us care about on the alternative meat side of things, but ultimately, we just want to provide a product to consumers that they gravitate to on their own, regardless of the considerations. Regardless of those externalities which we've discussed.

So how do we get there? The way that we get there, and certainly the framing that we take from the perspective of our science and technology team, is we really have to break out each of these three production platforms into their constituent parts. Now you can see here the fundamental... and we think about this almost in technology terms, or almost in software development terms... the technology stack of each of these different production platforms.

So, you'll see here the tech stack for plant-based meat, the tech stack for fermentation derived products, and the tech stack for cultivated meat. And what I'll do in the ensuing few slides, and with the remainder of my time, is I'll zoom in on one area of the tech stack of each of these three production platforms, to give you all an idea of how we think about these products and their horizons, and how we can optimize them, again, to reach those goals of price and taste parity.

So, we'll start out with plant-based meat. Now, as many of you all will be familiar, plant-based meat is not a new concept necessarily. And it's existed really in iterations for centuries, and in its current iteration for at least a decade or two. And historically, or at least over the past, say, 50 years, the way that plant-based meat has predominantly been produced is via an approach, a manufacturing approach, called extrusion. Now extrusion, again, as many of you all will know, was not initially developed and, and today is not exclusively used in the plant-based meat industry.

It was initially developed for the plastics industry. It has been used historically for manufacture of things like snacks. And we have essentially retrofitted extruders in order to turn plant proteins, typically plant protein isolates, or concentrates, into TVP or textured vegetable protein, really trying to replicate the experience of conventional meat. Now, the way that we do this via extrusion, both low and high moisture extrusion, is to apply pressure and heat. And then some degree of moisture, of course, in order to persuade those plant proteins, that plant protein concentrate or isolate, to act more like the fibrous protein which is typically found in animal meat.

The upside of course, with this kind of canonical or prevailing approach of extrusion that you'll see on the left is that we can produce it quite a high throughput. So, it seems to us to be quite a good solution right now, if we want to be able to produce a lot of plant-based meat to satisfy non-trivial percentages of that global meat market. Satisfy non-trivial percentages of that 350 million metric tons. But of course, there are frontiers, there are ways that we need to continue to optimize the texture and both... or excuse me, of both the texture and the flavors of the products that are extruded, the extrudates themselves.

There are also, of course, emerging technologies to manufacture plant-based meat. So, shear cell technology and spinning technologies are really just two of a variety of new generation approaches to texturizing plant proteins. To creating plant-based meats that bear organoleptic resemblance to conventional animal meats. Shear cell technology, quite an interesting approach, developed initially, I believe, out of Wageningen, a leading ag university in the Netherlands. Now this approach seems to be quite favorable, because we are able to better recapitulate the experience, the fibrous structure of conventional animal steaks, or whole muscle cuts.

And likewise spinning technology is, is potentially quite interesting in its application to plant-based meats. Of course, spinning technology emerging largely from the textiles industry, the weaving industries. And the theory, and potentially the practice, is that you can create these long fibrous, essentially strings of plant proteins, which are better replicating that fibrillar structure of conventional

meats, particularly steaks. As well, of course, we would be remiss not to mention 3D printing approaches.

Now, the reason why I mentioned the near-term stretch, question mark here, is not because of our questioning the ability to replicate the experience of conventional meat. Actually, 3D printing may be able to do the most precise job of faithfully recreating, creating a facsimile of say a steak, a filet mignon, if you will. But the question here, of course, with 3D printing, is always the throughput. It's always the volume, the production volume, how much of it can we produce? And can we produce at a price that is amenable to commoditized meat products? And so that is the main fundamental, or it's a fundamental question, at least for me when it comes to the 3D printing, but it's an interesting approach nonetheless, because right now it can likely get us as close as possible to the actual true experience of consuming conventional steaks.

Now, oftentimes when we think about the question of taste and plant-based meats, we initially gravitate, our minds initially, or at least for me gravitate towards, the flavor, the taste of plant-based meats. But ultimately, and as I've alluded to, we're not going to crack this code unless we optimize for texture. And I just wanted to show briefly an example here that some of you all may be familiar with. This is coming from a company called Juicy Marbles. There are other companies taking similar approaches in the industry as well. And they're using manufacturing approach, which I referenced on the last slide. But essentially, the upshot here is that, think about it.

This is a company that has existed for a few years, no more than two or three years. They've got a team of three to five people. And in that span of time, in that infinitesimally small span of time, they have been able to create a product that at least prima facie, on its face, it bears pretty striking resemblance to conventional steaks. And this is a team that was able to do this in a few years with not even a few million dollars.

Now expand this concept out using these technologies, these texturization technologies incorporating fats as well as muscles from plant proteins, a decade out, and extend that to hundreds of millions of dollars of R&D. Right? Put Impossible Foods and Beyond Meats' entire R & D teams and budgets on this question of steaks and imagine what we are going to be able to produce a decade out. If this is v1.0, the horizon is quite striking, and quite favorable in terms of its prospects. So, I won't go any deeper there on the plant-based side of things, in the interest of time, I will transition briefly to fermentation.

Now, as it pertains to fermentation, GFI really instantiated fermentation as a third pillar of the alternative protein industry last year, in our fermentation state of the industry reports, published in 2020, I recommend you check in and out if you want to go deeper on fermentation. What I will say here is that really, we categorize fermentation broadly as falling into three subcategories. The first is traditional fermentation.

Of course, traditional fermentation has been utilized for centuries, and actually millennia, essentially using microbes to modulate different food and beverage processes. Of course, brewing with beer, creation of cheeses and yogurts, but also for the purposes of plant-based meat, use of soybeans to modulate... or, excuse me, modulating soybeans with things like *Rhizopus*, so again, it's a strain of a microbe, in order to create Tempeh. And there are ways in which we can use this traditional fermentation approach to create better and better plant-based meats.

Likewise, there's biomass fermentation. Now biomass fermentation has existed actually for quite some time in the alt protein industry, largely by virtue of a company called Quorn, in the UK. They use a strain, to my knowledge, it's *fusarium v.*, in order to create a mycoprotein, which consumers have had access to for many decades. Now, some of the exciting frontiers, or actually I'll take a step back there. The exciting theoretical prospect of using mycoprotein in biomass fermentation, where the consumer is actually eating the cells, the microbial cells, the mycelium itself, is that mycelium by its very fundamental biology seems to better replicate that fibrillar structure of animal proteins, or proteins that are traditionally found in animals.

Therefore, this may be an interesting sub-sector if we are trying to optimize for whole muscle cuts of steak. There are companies that are innovating the next generation of biomass fermentation. That includes companies like Atlas Food Co., they spun out of Ecovative, as well as Emergy Foods in Boulder, both creating really compelling whole muscle cut prototypes. Now finally, I'll transition us to precision fermentation.

Now, precision fermentation is, as a technology, really synthetic biology in practice. And we have used precision fermentation in industries spanning from chemicals, enzymes, biofuels, and certainly in the biotherapeutics industry, using it to produce things like monoclonal antibodies. And here, as it applies to food, it is the theory, right, that we can take proteins that are traditionally found in animals, dairy proteins, egg proteins, et cetera, and code those genes into the genomes of microbes, and have the microbes produce those molecularly identical proteins and other molecules of interest.

So, it's basically a hacking of the biological system, and it's a way that we can create precise animal proteins without the animal itself. So, I want to home in just briefly on this concept of precision fermentation, this top bucket up here, and we'll look at three brief applications of precision fermentation. I briefly referenced them. And then just talk about some of the cost considerations.

So, a company like Perfect Day, and many others, are creating dairy proteins like whey via microbes, a company like Clara Foods in the bay as well. They're producing egg white proteins, things like albumen. And then Impossible Foods, which is traditionally really considered a plant-based company, of course their hero, or their magic ingredient, heme, is produced via precision fermentation as well. And they all use a variety of different... They likely use fungi, not bacteria. Most of them probably use *Pichia pastoris* or another common strain. But the upshot here is that they are able to produce proteins historically found in animals, but they're able to do so via microbes.

Now from a cost perspective, what we have to think about when we're trying to optimize this precision fermentation process, particularly as it applies to food, is the cost profile. And when it comes to the cost profile, there are two things that I'll highlight briefly here. One is the titer. This is basically the grams per liter that we are able to express those proteins in a given amount of microbes.

When we're thinking about the titer of these microbial expression systems, we really need to optimize their overall yield. Or well, the titer and the yield, if we are able to get, or if we are trying to get them to a price point that is competitive with conventional animal products. In addition to the titer, just the pure amount of protein that is expressed via these microbes, we must think about downstream processing, which really in many ways emerges as the main cost driver at scale of this precision fermentation process.

Now downstream processing, theoretically, is just the idea that you separate out the microbe that is expressing the protein from the protein itself. Say the whey, because we just ideally want to use whey, in some degree of purified format, to incorporate into various products. So, we may use technologies or techniques like centrifugation, to separate out those two sub buckets, the microbe and the protein of interest. And of course, we can use technologies like spray drying to actually create usable formats and powders of these different proteins.

And again, on the downstream processing side, in a variety of industries, if you think about biotherapeutics, these companies are oftentimes incentivized to create extremely high value proteins, because they're going in our bodies. But at the same time, they don't have to think as much, at least, about the cost considerations at the processing, because they're able to charge super high margins on their products. In the food industry, we really need to focus on either creating somewhat less pure products so we can reduce the cost profile or creating better systems for purifying proteins at a lower cost. Again, so that we're able to move down the cost curve.

Now, finally, I want to briefly talk about cultivated meat, animal cell culture, cell cultured meat, cell-based meat. You've probably heard all sorts of terms. The only ones that I won't particularly advocate for are lab grown meat and Frankenmeat, but I think that's for another discussion. So cultivated meat is, as many of you all will be familiar with as well, is the concept that we can take the cells directly from an animal. Typically, in the format of a biopsy, although we can engineer other cells, IPSEs and the like. Take cells from animals, and we proliferate them outside of the animal's body and ultimately are able to create a molecularly identical meat product, but just obviating the need for the actual animal husbandry.

This is often taking place in a bioreactor, likely a stirred tank bioreactor. And we are using not only muscle cells, which are found in meat, but fat cells, so adipocytes, as well as a variety of other cells, which are going to be necessary. Things like fibroblasts. I mean, satellite cells, there are a variety of additional cell lines that must be considered. But nonetheless, the basic theory is we take the cells from the animal. We proliferate them in high density, in a stirred tank bioreactor or something similar, and then ultimately use techniques developed from the tissue engineering space in order to perfuse or seed those cells onto a scaffolding, that will then recapitulate or create that experience of a meat product.

Again, in the interests of time, I won't go much deeper here, but I do want to talk about the key to cultivated meat. And again, this is the difference between cultivated meat being some scientific oddity that you hear about in a few journals, and then it fades away to the dustbin of history. Versus cultivated meat being the predominant way that we feed billions of people with meat, every single day for the millennia to come. And of course, the difference between those two bifurcated potential states is the cost.

And when it comes to costs, there are a variety of considerations. I will mention four of them here, and they emerged from a recent or actually a few recent techno-economic assessments of cultivated meat. One is we have to focus actually on quite a similar manner to the fact that we need to optimize the cell lines, the microbial cell lines for fermentation, we must focus on metabolic engineering approaches in cultivating meat, to increase the sales potential for high density culture.

There are considerations around viscosity. There are considerations around ensuring that we are limiting the CO₂ in the cell culture, or in the bioreactor. This is because CO₂ can inhibit cell growth, and ultimately kill the cells. And ensuring that the cells themselves in the bioreactor have access to sufficient

oxygen, and then inhibiting, as well, various catabolites that are produced as a result of the cell culture and proliferation.

Likewise, cell culture media. Cell culture media is right now a predominant cost driver of cell cultured, or cell based, or cultivated meat. When it comes to media there are a variety of different discussions that that need to be had, and research projects that need to be undertaken. One that I think is particularly interesting and tractable is the concept of sourcing amino acids that will comprise the cell culture media from plant hydrolysates. Right now, the industry that predominantly uses cell culture media, the bio-pharmaceutical industry, the life sciences industry, isn't terribly incentivized, if you will, to reduce the input costs of media.

Because again, they're playing in a relatively high value market, with relatively low volumes of media. When it comes to cultivating meat, we're flipping that paradigm on its head, and we are producing, or we intend to produce in extremely high volumes, right? Hundreds or millions of metric tons. And at an extremely low value, right? We are trying to produce commoditized meat. In order to do so, one opportunity to reduce costs is actually to use various plant proteins. Again, things like soy protein and source amino acids from them so that they will ultimately be cheaper inputs into cultivating meat.

We can also, just briefly here, look at strategies like media recycling to reduce the overall cost of goods sold. And it's important to recognize as well that as cultivated meat scales up, today, it's at about pilot scale. We intend for within the next five to seven years, for it to really move into industrial scale production. Well, once we move cultivated meat into industrial scale production, the facility cap ex, the capital expenditure, the steel in the ground, the pipes, et cetera, that will become a predominant cost driver of cultivated meat, the unit price, in the same way that it made in the biofuels industry. And we have to find ways to reduce the facility capital expenditure if this is going to be a feasible investment for investors, for capital providers who are looking to supply this industry.

So, I will round us out on this one last slide. And I just want us to take a holistic look of these three different production platforms for plant or excuse me for alternative protein production. And think about them on these two metrics here, organoleptics, the ability to replicate the experience of conventional meat, or ultimately beat the experience of conventional meat, and then also price. How can we produce it super cheap?

Right now, if you look on the right side, plant-based meat from a price standpoint, we think we can get to price competitiveness with conventional meat really within the next few years. The question is, can we increase, can we improve the organoleptics of these products, to a point where we are again, indistinguishable or even better from conventional meat? The question of cultivating meat of course, is, one we think, theoretically, and from the products that we've tried, that these products will be organoleptically, identical to conventional meat products. That's the promise, it's the holy grail.

But at the same time, we have to ensure that cultivated meat moves down this price curve here, so that it is ultimately competitive from a pricing standpoint with the conventional meat industry. Lastly, fermentation. It does an incredible job of molecularly creating, recreating animal proteins. But again, it's a reasonably expensive process right now. Can we move down the cost curve so that these products are better able to compete with conventional meat products?

Last thing that I'll say is we talk about these three separate buckets. Already today, Impossible Foods, their burger is a hybrid between fermentation and plant based. Perfect Day, in their ice cream, is a

hybrid between their precision fermentation whey and their plant-based other ingredients in their ice cream. These three categories will eventually essentially merge. And so, we will think about them really as one unit, as opposed to three separate pillars. So, with that, I will yield my time to the floor, and I welcome any questions.