THE GOOD FOOD INSTITUTE

State of the Industry Report

Fermentation:

An Introduction to a Pillar of the Alternative Protein Industry

Photo credit: Meati.

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What is the role of fermentation in the context of alternative proteins?

Fermentation has been used in food production for millennia. Ancient civilizations used microbial cultures to preserve foods, create alcoholic beverages, and improve the nutritional value and bioavailability of foods ranging from kimchi to tempeh. Over the past century, the role of fermentation has expanded far beyond its historical usage to a much broader range of applications, spanning industrial chemistry, biomaterials, therapeutics and medicine, fuels, and advanced food ingredients. The suite of tools developed through fermentation's technological evolution is now poised to revolutionize the food sector by enabling and accelerating the rise of alternative proteins.

The term "fermentation" carries distinct meanings across different disciplines. Within biology, it refers to a specific metabolic pathway used to generate energy in the absence of oxygen. However, it has taken on a more generalized definition in food and industrial biotechnology that aligns more closely with fermentation's use in alternative proteins. In the alternative protein industry, "fermentation" refers to cultivating microbial organisms for the purpose of processing a foodstuff; obtaining more of the organism itself as a primary source of protein; or deriving specialized ingredients, such as flavorings, enzymes, and fats, for incorporation into plant-based products or cultivated meat.

The alternative protein industry uses fermentation in three primary ways:

1. **Traditional fermentation** uses intact live microorganisms to modulate and process plant-derived ingredients, resulting in products with unique flavor and nutritional profiles and modified texture. Examples are using the fungus *Rhizopus* to ferment soybeans into tempeh and various lactic acid bacteria to produce cheese and yogurt, as well as more modern renditions of this concept, such as MycoTechnology's fermentation of plant-based proteins to improve flavor and functionality.

2. **Biomass fermentation** leverages the fast growth and high protein content of many microorganisms to efficiently produce large quantities of protein. The microbial biomass itself serves as an ingredient with the cells intact or minimally processed—for example, with the cells broken open to improve digestibility or to enrich for even higher protein content, akin to processing plant flours into protein concentrates and isolates. This biomass serves as the predominant ingredient of a food product or as one of several primary ingredients in a blend. Examples of biomass fermentation are Quorn's and Meati's use of filamentous fungi as the base for their meat analogs.

Notes that appear in boxes in the margins throughout the document are a descriptor of the words underlined in orange in the main text.

Bioavailability
A measure of the degree to which a nutrient can be absorbed by the body during digestion. Even if high nutrient content is present in a food, it may not all be accessible or digestible, meaning that delivery of nutrients may be compromised unless the bioavailability is also high.

Enzymes
Proteins that catalyze biochemical reactions, such as breaking chemical bonds or creating new bonds, often with high specificity. Common uses of enzymes in food include breaking down undesirable or insoluble components and crosslinking ingredients to improve texture.

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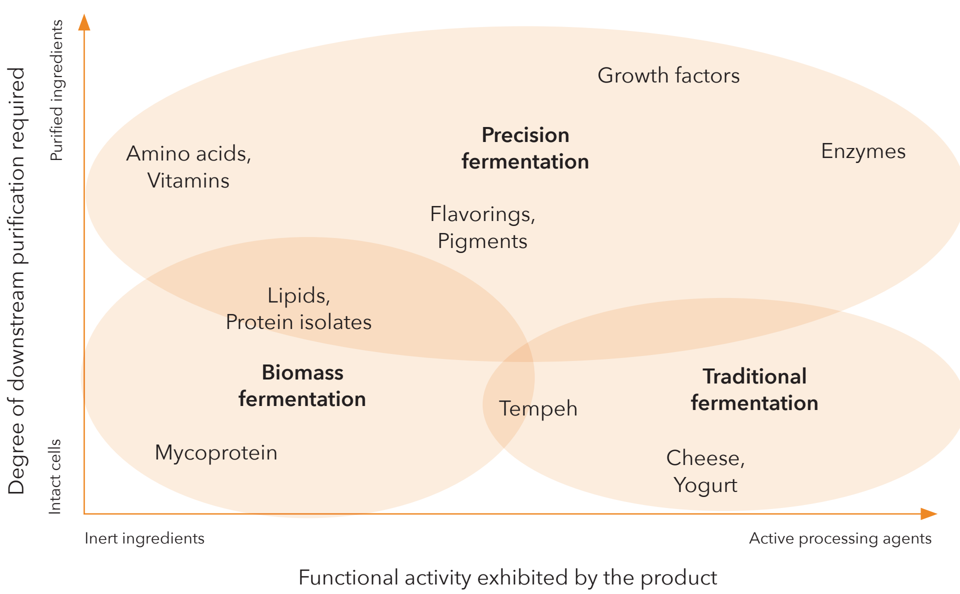
3. **Precision fermentation** uses microbial hosts as "cell factories" for producing specific functional ingredients that typically require greater purity than the primary protein ingredients and are incorporated at lower levels. These functional ingredients are powerful enablers of improved sensory characteristics and functional attributes of plant-based products or cultivated meat. Examples are proteins, such as Perfect Day's dairy proteins, Clara Foods' egg proteins, and Impossible Foods' heme protein; enzymes; flavoring agents; vitamins; natural pigments; and fats.

Innovations are occurring across all three uses. Figure 1 conceptually segments these uses along two axes. The vertical axis indicates the degree to which the fermentation-derived or fermentation-enabled product requires downstream fractionation and purification. The horizontal axis reflects the degree to which the product acts as a functional, active processing agent within the final product formulation.

This biaxial landscape charts examples that are illustrative, not comprehensive; individual manifestations of each product category may result from somewhat different approaches that would warrant adjusting their placement on this conceptual map. It should be noted that a single product can span multiple categories across fermentation segments. For example, a microorganism used for biomass fermentation or traditional fermentation can also be engineered to produce a high-value ingredient via precision fermentation, thus contributing the high-value ingredient to the final product without the need for downstream purification.



Source: GFI.

FIGURE 1. A conceptual landscape of fermentation-derived and fermentation-enabled products.

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Traditional fermentation: Leveraging the power of biology to transform food ingredients

Historical examples of fermentation (alcohol, tempeh) cluster near the bottom of the degree of purification axis and on the right side of the biological activity axis in Figure 1. These are products of cells used as living biological processing units to convert raw materials into more desirable forms. In the case of tempeh, fungal mycelium is grown on soybeans (or other pulses or grains) to break down antinutritional factors, improve nutritional content, and enhance the flavor profile. During its growth and metabolism, the fungus processes the soybean feedstock, but it also remains in the final product, adding to the flavor and texture and thus functioning as both an ingredient and an active processing mechanism.

By contrast, bacterial cultures used to produce cheese and yogurt excrete a host of metabolites that modulate flavor and texture during culturing. While the cells serve probiotic functions upon ingestion, they themselves do not contribute substantially to the final product as an ingredient.

Traditional fermentation has been widely used for millennia. Only since the 1980s have biomass fermentation and precision fermentation meaningfully emerged in the food industry. But while traditional fermentation may at first appear relatively "low-tech," it offers abundant room for innovation, such as adapting microbial strains to new plant-based inputs or selecting for strains with enhanced flavor profiles.

In addition to serving its familiar purpose in consumer-facing products such as yogurt and tempeh, traditional fermentation can improve the performance of plant-based ingredients—for example, by removing bitterness from plant proteins. **PLANETARIANS'** products exemplify fermentation's role as a functionality-enhancing technology in plant-based meat production. The company uses fermentation to improve the digestibility, taste, texture, and nutritional profiles of otherwise low-value agro-industrial byproducts, such as pressed sunflower cakes. Similarly, meat industry leader JBS's new brand, Planterra Foods, just **launched** a line of plant-based meat products using rice and pea protein fermented by shiitake mycelium from MycoTechnology. Thus, traditional fermentation can be leveraged as a bio-based alternative to chemical or mechanical methods of enhancing plant protein performance.

Mycelium
The vegetative structure of filamentous fungi. Mycelium is a matrix of thin, fibrous strands called hyphae that serve as the roots, in a sense, of many types of fungi—including fungi that form mushrooms as fruiting bodies. These strands secrete enzymes to digest and absorb the biomass on which the fungus is growing. This is how fungi acquire nutrients.

Antinutritional factors
Components that can interfere with absorption of nutrients, thus lowering their bioavailability.

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Biomass fermentation: Microorganisms' great promise as protein powerhouses

Many microorganisms offer innately high protein content (over 50% by dry weight for many fungal, bacterial, and algal species) coupled with extraordinarily fast and self-sufficient growth, requiring only simple and inexpensive nutrient feedstocks. While the generational cycle of animals raised for meat is on the order of months to years, and crop plants typically require growing seasons of weeks or months, the doubling time of most microorganisms is hours or even minutes. Cell culture processes, such as fermentation, capitalize on the fundamental biological property of exponential growth, meaning that every growth cycle can double the available biomass. When performed at the scale of hundreds of thousands of liters, these processes generate **tens of metric tons** of biomass *every hour*.

Doubling time
The time it takes for a population to double in size. In the context of cell culture, this corresponds to the rate at which cells divide.

The concept of single-cell protein has been attractive from the perspective of food security and sustainability since at least the 1960s, and products such as Marmite (inception 1902) are among the first uses of microbial biomass itself as a human food. However, Quorn was the first company to commercialize microbial biomass for use in products intended to substitute for meat products. For decades Quorn was the only real contender in this space, but new entrants recognize the potential of biomass fermentation. Filamentous fungi (including the strain used by Quorn, *Fusarium venenatum*) offer additional benefits for texture in recapitulating the fibrous structure of meat products. Innovators are exploring unconventional species, as well as new feedstocks and bioprocess designs, to further improve the efficiency, sustainability, and economy of the process while pursuing consumer-relevant attributes, such as taste and texture.

Precision fermentation: Harnessing microbial hosts as cell factories

This fermentation category has been well established in the food industry for many years, but innovators are now investigating novel solutions tailored to the specific needs of the alternative protein industry. Biology provides food developers with an almost boundless palette of molecules from which to assemble flavors, textures, and aromas. However, not all these ingredients are easily sourced at large volumes and low prices. Theoretically, using microbial cells as the production host, precision fermentation allows for highly scalable manufacture of virtually any ingredient. Indeed, fermentation-derived ingredients are already widely used across the food industry. For instance, the majority of vitamins in nutritional supplements and fortified processed foods, such as B12 and riboflavin, are produced through fermentation, as are many flavoring components.

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Highly purified fermentation-derived components are perhaps most visibly used in alternative protein products as functional ingredients. In fact, the food industry was among the first to leverage fermentation to displace animal products in everyday use. Commercialization of recombinant chymosin in the 1980s rendered calf rennet's vital use as a coagulant in cheesemaking obsolete for most global cheese production. Chymosin, the major enzyme in calf rennet, is otherwise produced in the lining of calves' stomachs. A notable recent example is Impossible Foods' use of purified soy leghemoglobin, produced with *Pichia pastoris*, as a flavoring ingredient and catalyzer in their burger. These functions combine to produce a suite of organoleptic properties in the cooked product—most notably, the red color and "bloody" taste that has made Impossible Burger a paradigm for innovation in functional ingredients.

Other recombinant proteins, such as casein and whey, are highly purified and exhibit melting and stretching functionality. These proteins and plant-derived ingredients can combine to create a final product. For example, sugar, coconut oil, and sunflower oil combine with recombinant whey to make Perfect Day's ice cream base.

The same symbiosis exists between fermentation and cultivated meat. In fact, fermentation is the primary means of producing animal-origin-free growth factors to replace those of animal origin in cultivated meat production. Several companies, including **ORF Genetics**, **Richcore**, and **Peprotech**, already work in this space. Furthermore, proteins such as collagen or fibronectin produced through fermentation may serve as key animal-free components of scaffolding for more complex cultivated meat products.

Thus, although fermentation is valued as an efficient and scalable method of producing high-quality protein, its powerful force-multiplying effect on the cultivated meat and plant-based meat, egg, and dairy industries is perhaps underappreciated.

Functional ingredients
Bioactive compounds that enhance the sensory aspects, nutritional properties, shelf stability, cooking attributes, and other target characteristics of a food product.

Organoleptic
Pertaining to the senses, including taste, smell, sight, and touch.

Growth factors
Signaling molecules used in animal cell culture to guide cell growth and differentiation. Historically these were often sourced from animal serum, but they can also be produced through precision fermentation.

The power of fermentation

We are still in the early days of the transition to a post-animal food production system. As plant-based meat, egg, and dairy products become more ubiquitous, so will fermentation-enabled alternatives. Fermentation, whether traditional, precision, or biomass, offers to support product development across the alternative protein landscape by scaling production of unique ingredients.

By virtue of versatility, fermentation merits inclusion as a pillar of the alternative protein industry. While fermentation has a rich history of use in food, as the modern era has demonstrated, its innovative potential is still largely untapped.

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Innovations in fermentation will improve plant-based products and cultivated meat, in turn increasing demand and market opportunity—leading to a virtuous cycle of growth in the alternative protein industry. Additionally, the benefits of fermentation to human health and the environment are likely to be key drivers of adoption by consumers and producers.

Mycelium, microalgae, microbes, and fermented plant proteins can provide the sensory experiences and full nutritional profiles of animal products but without undesirable substances, such as cholesterol, antibiotics, and hormones. Fermentation's ability to efficiently produce protein could resolve the **global protein deficit**. Fermentation will enable companies to meet the growing demand for protein at a cost that is competitive with or lower than that of animal products and potentially lift millions out of malnutrition. This protein could be both less expensive to produce and higher quality than animal proteins. A 2019 University of Exeter **study** found that athletes who consumed Quorn's mycoprotein after strenuous exercise "increased their muscle growth rates by more than double" the rate of athletes who consumed milk protein afterward. Mycoprotein, the main ingredient in all Quorn products, is thus more effective at promoting muscle growth than milk protein. Mycoprotein's PDCAAS protein digestibility score is **as high or higher** than those of ground beef, pea protein, insect protein, and soy protein.

Efficient protein production is good not just for human health but for planetary health. Microbes are **much more efficient than livestock** at converting calories into protein and high-value molecules (reducing pollutants and GHG emissions and saving water and land) and can consume a wider variety of feedstocks. These feedstocks are often low-cost industrial or agricultural side streams or waste streams. This lowers both variable and external costs associated with production, such as transportation of inputs. Feedstock diversification will enable local production that leverages readily available feedstocks without long-distance shipping. Companies will explore more ways to convert low-value local byproducts, such as spent grain or corn husks, into high-value proteins or even develop fully circular production processes.

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The Good Food Institute (GFI) is pleased to present this first-of-its-kind report as an introduction to and potential roadmap for fermentation technology's use in the alternative protein industry. GFI is a 501(c)(3) nonprofit powered by philanthropy. Our mission is to transform the food system into one that is more sustainable, healthy, and just. Fermentation is a key component in realizing our vision, and this report provides an overview of the companies, technologies, and investments driving the industry forward. Section 2 outlines the competitive landscape, and sections 3 and 4 examine the end-product and ingredient use cases for fermentation, respectively. Section 5 covers investment trends, the top companies by venture capital raised, and the most active investors in the space. Section 6 is a deeper dive into the fermentation-technology value chain and the innovation opportunities along it. Finally, Section 7 highlights regulatory updates and nomenclature for this burgeoning industry.

Source: Atlast Food Co.

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Overview

Fermentation's plethora of uses across food and other sectors has drawn tremendous corporate investment in diverse applications and production capacity. Several hundred companies now use fermentation to generate hundreds of billions in annual revenue while improving the lives of millions around the world (e.g., diabetics who rely on recombinant insulin). As interest in alternative proteins has grown in the past several years, many of these companies, as well as smaller startups, have diversified and created business initiatives in the alternative protein industry (Table 3). Equally exciting is the formation of at least 44 new companies focused primarily on fermentation for use in alternative protein applications (Table 2).

Competitive landscape

Creation of proteins, lipids, and functional ingredients for meat, egg, and dairy alternatives is one of the newest and most promising applications for fermentation. GFI has identified 68 companies using fermentation to produce or support animal-free formulations of meat, eggs, and dairy or their functional equivalents (e.g., a fermentation-derived ingredient to replace eggs in baking). These 68 represent only publicly disclosed projects, so the actual number could be much higher. They range from the largest life sciences companies to nascent spinouts from PhD theses.

Their initiatives are generally divided into "traditional fermentation," "biomass," and "functional ingredients" (produced via precision fermentation) (Figure 1). The line between biomass and functional ingredient is not always clear. Some biomass products also impart special functionality to the end product, and some functional ingredients make up a significant portion of an end product's mass. These proteins, as well as fats and other compounds, are best considered along a spectrum. Companies use a variety of organisms, feedstocks, technology platforms, and business strategies to enable or create a broad swath of products. Figure 2, a non-exhaustive "mind map" of the fermentation sector as it relates to alternative proteins, highlights this landscape of possibilities.

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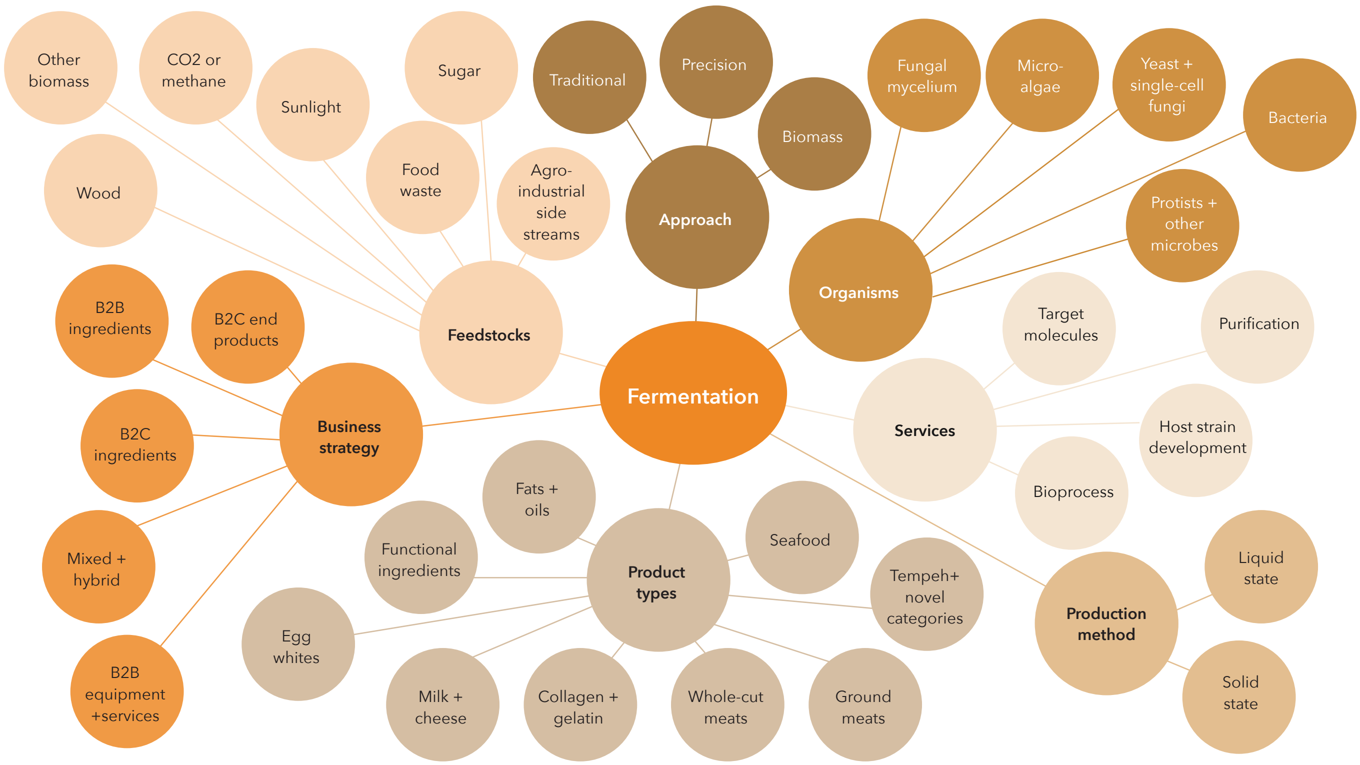

FIGURE 2. Mind map: A visual representation of the landscape of fermentation within alternative proteins.

The following tables provide an overview of companies working in alternative protein fermentation either as their core function (Table 2) or as an initiative of a broader business (Table 3). All company references are purely illustrative, and these lists are not exhaustive. Rather, they offer a snapshot of the diverse companies and technology applications for fermentation. Because of fermentation technology's broad uses, Table 1 sets parameters for inclusion in this section and in Section 5 on investments.

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TABLE 1. Report scope: Types of companies included

Type of company, activity, or product	Included in the competitive landscape chart?	Included in investment calculations?
Microbes (bacteria, microalgae, protists, and single-cell fungi to produce edible biomass or functional ingredients for plant-based meat, eggs, and dairy, as well as ingredients for meat cultivation (e.g., growth factors)	Yes	Yes, if fermentation for alternative protein applications is their primary business function
Mycelium to produce edible biomass or functional ingredients for plant-based meat, eggs, and dairy	Yes	Yes, if fermentation for alternative protein applications is their primary business function
Business-to-business support to fermentation companies working in alternative proteins	Yes	Yes, if fermentation for alternative protein applications is their primary business function
Fermentation to produce food ingredients that are not a replacement for meat, eggs, or dairy (e.g., sweeteners, protein powders)	No	No
Fermentation to produce non-human or non-pet food items and other molecules (e.g., biofertilizer, animal feed, aquaculture feed, chemicals, biofuel, cosmetics, biologics)	No	No
Fermentation to produce pet food	Yes, because of the high degree of relevance to human food applications in the future and the displacement of meat products	Yes
R&D happening within large corporations that is not publicly disclosed (as well as startup companies in "stealth mode")	No	No
Nut (and other fermented) cheese and butter (e.g., Miyoko's)	No, covered in GFI's state of the industry report on plant-based meat, eggs, and dairy	No
Tempeh and other traditional fermented foods like sourdough or kimchi (e.g., Better Nature and SunRhize)	No, covered in GFI's state of the industry report on plant-based meat, eggs, and dairy	No
Macroalgae (e.g., kelp, seaweed, dulse, sea vegetables)	No, covered in GFI's state of the industry report on plant-based meat, eggs, and dairy	No
Mushrooms (the fruiting bodies of some fungi)	No, covered in GFI's state of the industry report on plant-based meat, eggs, and dairy	No
Nonprofit organizations and academic research labs	No	No
Companies with current applications of fermentation technology for alternative proteins and lipids but as part of a broader business	Yes	No, because we cannot verify the percentage of investment dollars going to applications within this scope

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Of the 44 companies focused primarily on fermentation for alternative protein applications, 18 are biomass companies, 21 precision fermentation companies, and five traditional fermentation companies. Countless other traditional fermentation companies exist (e.g., cheesemakers, tempeh makers, and brewers), but this report covers only those using traditional fermentation in a novel way, such as combining it with extrusion to create plant-based meat analogs. These 44 companies use a diverse landscape of production platforms, organisms, and feedstocks to deliver protein; fat; and functional elements, such as structure and texture, for a broad set of animal-free meat, egg, and dairy products as shown in Table 2.

TABLE 2. Companies focused on fermentation for animal-free meat, eggs, and dairy (alphabetized)

Company name	Brief description	Location	Founders	Year founded	Total investment*	Technology category
3F Bio	Mycoprotein production process for meat alternatives and protein ingredients	Glasgow, Scotland, UK	Craig Johnson, David Ritchie, Jim Laird	2015	$9.22 million (Series A)	Biomass
Afineur	Fermentation-derived protein for plant-based foods	New York, NY, USA	Camille Delebecque, Sophie Deterre	2014	$0.22 million (accelerator/ incubator)	Traditional, biomass
Air Protein	Alternative meat (chicken, beef, pork) and seafood transformed from CO2	Berkeley, CA, USA	Lisa Dyson	2019	N/A	Biomass
Algama	Platform for microalgae-based foods and ingredients (including egg, seafood, meat, and dairy replacements)	Paris, France	Alvyn Severien, Gaëtan Gohin	2016	$9.56 million (Series A)	Biomass
Atlast Food Co	Whole-cut mycelium-based meats (starting with bacon)	Green Island, NY, USA	Eben Bayer, Steve Lomnes, Russell Hazen, Gavin McIntyre, Andy Bass, Alex Carlton	2019	$7 million (seed)	Biomass
Bond Pet Foods	Microbially produced animal proteins for pet food	Boulder, CO, USA	Rich Kelleman, Pernilla Turner Audibert	2015	$1.2 million (seed)	Precision
BTFRY	Prototyping for mycelium use in plant-based snacks, supplements, and meat alternatives	Chicago, IL, USA	Justin Whiteley	2018	N/A	Biomass
Change Foods	Proteins and fats for dairy (starting with cheese)	San Francisco, CA, USA	David Bucca	2019	N/A	Precision

*Total investment, last round type (PitchBook).

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Circe	Fermentation of dairy triglycerides and synthetic polymers (spinout of Wyss translation program)	Boston, MA, USA	Shannon Nangle, Marika Ziesack, Kevin McDonough	2020	N/A	Precision
Clara Foods	Egg proteins through fermentation	San Francisco, CA, USA	Arturo Elizondo, David Anchel	2014	$56.80 million (Series B)	Precision
Cultivated	Alternatives to dairy products through microbial fermentation	Lausanne, Switzerland	Tomas Turner, Denis Joly	2020	N/A	Precision
Final Foods	Whey proteins for cheese produced by yeast in open source bioreactor	Santa Clara, CA, USA	Julian Ramirez, Marco Graziano, Barbara Dunn	2020	N/A	Precision
Foods Myco Mizoram	Mycelium-derived meat	Aizawl, India	Henry Saingura	2019	N/A	Biomass
Fumi Ingredients	Egg replacement ingredient through microbial fermentation	Wageningen, Netherlands	Edgar Suarez Garcia, Corjan Van den Berg	2019	$0.60 million (seed)	Precision
Fybraworks Foods	Mycelium as an expression platform for animal muscle proteins for meat alternatives	Minneapolis, MN, USA	Chenfeng Lu, David Liu	2020	N/A	Precision
Harmony	Infant formula using human milk proteins produced via fermentation	Boston, MA, USA	Wendel Afonso	2020	N/A	Precision
Helaina	Infant formula using human milk proteins produced via yeast	New York, NY, USA	Laura Katz	2020	N/A	Precision
Imagindairy Ltd.	Development of milk proteins with AI platform and fermentation	Israel	Eyal Afergan, Tamir Tuller	2020	$850,000	Precision
Kernel Mycofood	Decentralized production of mycoprotein	Buenos Aires, Argentina	Horacio Acerbo, Martin Blasco, Lucas Gago, Sebastian Taito, Miguel Neumann	2019	N/A	Biomass
Kinoko-Tech	Mycelium-derived meat producer	Rehovot, Israel	Daria Feldman, Hadar Shohat, Jasmin Ravid	2019	N/A	Biomass
LegenDairy Foods	Milk proteins for dairy products using microbes	Berlin, Germany	Raffael Wohlgensinger	2019	$4.43 million (seed)	Precision
Meati (formerly Emergy Foods)	Whole-muscle meats made from mycelium, including steak, chicken, and fish	Boulder, CO, USA	Justin Whiteley, Tyler Huggins	2016	$7.17 million (seed)	Biomass

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Mediterranean Food Lab	Novel methods inspired by traditional fermentation technologies to produce plant-based products and improve the sensory qualities of a wide range of plant-based meats and other foods	Tel Aviv, Israel	B.Z. Goldberg, Omer Ben Gal	2019	<$500,000 (seed)	Traditional
More Foods	Yeast-based meats	Tel Aviv, Israel	Leonardo Marcovitz	2019	N/A	Biomass
Motif FoodWorks	Functional ingredients, ingredient systems, and whole formulations for plant-based foods	Boston, MA, USA	Jonathan McIntyre	2018	$117.50 million (Series A)	Precision
Mushlabs	Mycelium-based ingredients for meat alternatives	Berlin, Germany	Mazen Rizk	2018	Undisclosed (seed)	Biomass
Mycorena	Industrial side streams into fungi-based protein for food applications (e.g, Swedish meatballs)	Gothenburg, Sweden	Ramkumar Nair	2017	$1.78 million (seed)	Biomass
MycoTechnology	Fungi-based bitter blocker ingredient and protein	Aurora, CO, USA	Alan Hahn, Brooks J. Kelly, James P. Langan, Peter Lubar	2013	$120.67 million (Series D)	Traditional
Nature's Fynd	Edible protein through cultivation of extremophile organisms through liquid air interface fermentation	Chicago, IL, USA	Thomas Jonas, Matthew Strongin, Mark Kozubal	2014	$113.00 million (Series B)	Biomass
New Culture	Casein for cheese production (starting with mozzarella)	San Francisco, CA, USA	Inja Radman, Matt Gibson	2018	$3.70 million (seed)	Precision
Nourish Ingredients	Fermentation-derived fats for meat, dairy, and fish alternatives	Brisbane, Australia	Ben Leita, James Petrie	2019	N/A	Precision
novacca	Milk proteins using fermentation platform	Nivå, Denmark		2018	N/A	Precision
Perfect Day	Milk proteins using fermentation platform	Berkeley, CA, USA	Perumal Gandhi, Ryan Pandya	2014	$360 million (Series C)	Precision
PLANETARIANS	Fermentation of plant-based meats from sunflower cakes to improve functionality	Palo Alto, CA, USA	Aleh Manchuliantsau, Anastasia Tkacheva	2017	$0.85 million (seed)	Traditional
Prime Roots	Meat analogs made from mycoprotein	San Francisco, CA, USA	Joshua Nixon, Kimberlie Le	2017	$4.50 million (seed)	Traditional
Provenance Bio	Synbio tools to create animal proteins (e.g., collagen for cultivated meat)	San Francisco, CA, USA	Christian Ewton	2016	Undisclosed (seed)	Precision
Pura	Mycoprotein production and fermentation to enhance plant-based foods	Inarzo, Italy	Stefano Babbini	2019	N/A	Biomass

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Quorn	Pioneering mycoprotein meat alternatives	Stokesley, England, UK	Lord Rank	1985	Undisclosed (acquisition by Monde Nissin)	Biomass
Remilk	Fermentation-derived dairy molecules	Tel Aviv, Israel	Aviv Wolff, Ori Cohavi	2019	Undisclosed (seed)	Precision
Solar Foods	Electrolysis-enabled novel protein under Solein brand for food ingredients, plant-based meat alternatives, and cultivated meat	Helsinki, Finland	Pasi Vainikka, Juha-Pekka Pitkanen	2017	$2.46 million (seed)	Biomass
Sophie's BioNutrients	Microalgae R&D to create proteins for plant-based meat and dairy	Singapore	Eugene Wang, Kirin Tsuei, Barnabas Chan	2013	N/A	Biomass
The Protein Brewery	Fungi-based protein to replace meat under the Fermotein brand and fungi-produced egg proteins	Breda, Netherlands	Wim de Laat	2019	Undisclosed (seed)	Biomass
Triton Algae Innovations	Heme and other meat-like compounds from microalgae for plant-based meat applications	San Diego, CA, USA	Miller Tran	2013	$5.00 million (seed)	Precision
Wild Earth	Fermentation-derived pet food	Berkeley, CA, USA	Ryan Bethencourt	2017	$4.55 million (seed)	Biomass

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At least 24 additional companies have formal projects in alternative proteins or product lines explicitly intended for the alternative protein industry. These companies span seven countries on three continents, but the largest concentration is 10 companies in the United States. Except for a few traditional fermentation companies, about half these companies work in biomass fermentation and half in precision fermentation. About half are startups (formed in the past 10 years) and half established corporations, including some of the world's largest food companies. Nearly all these companies are pursuing a business-to-business (B2B) strategy, which will be a valuable force multiplier for the industry because their expertise will benefit multiple clients rather than stay siloed in a single company.

TABLE 3. Companies with fermentation initiatives for animal-free meat, eggs, and dairy (alphabetized)

Company name	Brief description	Location	Founders	Year founded	Total investment*	Technology category
Arbiom	Fermentation of wood pulp into protein for plant-based meat applications	Durham, NC, USA	Marc Chevrel (CEO)	2017	N/A	Biomass
Arzeda	Synthetic biology and computational protein design to create designer fermentation strains with applications in agriculture and ingredients	Seattle, WA, USA	Alexandre Zanghellini, Daniela Grabs, Eric Althoff	2008	$16.45 million (Series A)	Precision
Biorealize	Platform for running fermentation experiments in food, cosmetics, and brewing	Philadelphia, PA, USA	Orkan Telhan, Michael Hogan, Karen Hogan	2015	$0.3 million (seed)	Precision
Biosyntia	Vitamins for plant-based food and other sectors	Copenhagen, Denmark	Andreas Laustsen, Morten O. A. Sommer	2012	$6.63 million (Series A)	Precision
BioTork	Microalgae omega-3 fatty acids	Gainesville, FL, USA	Eudes De Crecy	2008	$2.86 million (seed)	Precision, biomass
CJ Bio	Plant-based amino acids for flavoring of plant-based meats	Seoul, South Korea	Sin Ho Kang	1950	N/A	Precision
DuPont	Fermentation-derived probiotics for plant-based food and other applications	Wilmington, DE, USA	Edward Breen (CEO)	1802	N/A	Precision, biomass
Fermentalg	Microalgae for plant-based foods	Libourne, France	Pierre Calleja	2014	Public (PAR: FALG)	Biomass

*Total investment, last round type (PitchBook).

Geltor	Collagen/gelatin using fermentation platform	San Francisco, CA, USA	Alexander Lorestani, Nick Ouzounov	2015	$77.52 million (Series B)	Precision
Lallemand	Variety of yeasts and bacteria for plant-based meat, egg, and dairy applications, as well as growth factors and fermentation ingredients	Toronto, Canada	Jean Chagnon (President)	1895	N/A	Precision, biomass
Lesaffre	Yeast lines for human nutrition and applications in plant-based food	Marcq-en-Barœul, France	Antoine Baule (CEO)	1852	N/A	Biomass
Noblegen	Egg replacement powder from protist under the brand Eunite, proteins, and oils	Peterborough, Canada	Adam Noble, Andressa Lacerda	2013	$26.07 million (Series B)	Biomass
Novozymes	Fermentation services to extract protein from and enhance flavor in vegetables	Bagsværd, Denmark	Glenn E. Nedwin	2000	Public (CSE: NZYM B)	Precision, traditional
Odontella	Microalgae-based salmon under the brand name Solmon	Bordeaux, France	Pierre Calleja	2016	$0.58 million (seed)	Biomass
Peprotech	Recombinant proteins, including growth factors for cultivated meat	Rocky Hill, NJ, USA	N/A	1988	N/A	Precision
RhYme Biotechnology	Lipid-based ingredients for alternative proteins	Vancouver, Canada	Raphael Roccor, James Round	2016	N/A	Precision
Richcore Lifesciences	Recombinant proteins, including growth factors for cultivated meat	Bangalore, India	Subramani Ramachandrappa	2001	$12.97 million (Series B)	Precision
Shiru	High-value functional food proteins identified via a computational platform and created through precision fermentation	Berkeley CA, USA	Jasmin Hume	2019	$3.5 million (seed)	Precision
Spira	Spirulina for applications in plant-based food as a colorant, umami flavorant, protein isolate, texturizer, and binder	Los Angeles, CA, USA	Elliot Roth	2016	$0.59 million (seed)	Biomass
String Bio	Methane converted to other materials, including alternative protein applications	Bangalore, India	Ezhil Subbian, Vinod Kumar	2013	Undisclosed (seed)	Precision
TerraVia	Microalgae protein for plant-based food fortification, including the AlgaVia brand powder, to reduce the need for dairy, eggs, and oils in recipes	San Francisco, CA, USA	Jonathan S. Wolfson, Harrison Dillon	2012	$357.92 million (acquisition)	Biomass

Section 2: Companies

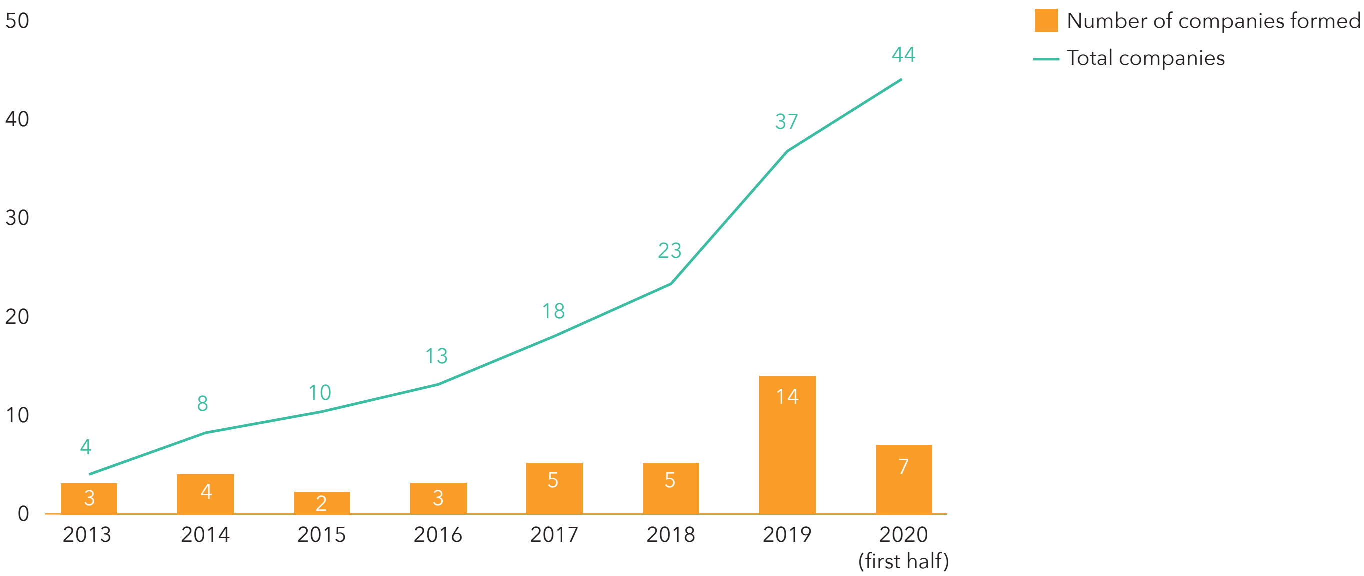
Tnuva	Series of soy yogurts enriched with bacteria	Israel	Eyal Malis (CEO)	1926	N/A	Traditional
Utilization of Carbon Dioxide Institute Co., Ltd.	Conversion of CO_2 and hydrogen to edible protein and other applications	Tokyo, Japan	Hideaki Yukawa (CEO)	2015	N/A	Biomass
White Dog Labs (Brewed Foods)	Bacteria-based protein "Plentify" and cheese "Eesy Cheese"	New Castle, DE, USA	Jonathan Gordon, Bryan Tracy	2012	$24.10 million (Series C)	Biomass

Are we missing something? Let GFI know by emailing **startup@gfi.org**.

Age and geographic scope

For much of their history, plant-based meat, eggs, and dairy were niche products aimed at feeding a small population of vegans and vegetarians. However, early innovators in the "plant-based 2.0" movement leveraged new ingredients and production methods, prompting wide interest in animal-free products among flexitarians. Quorn, founded in 1985, is an early innovator in the creation of meat analogs from fermentation-derived biomass. Impossible Foods, founded in 2011, is the first company to harness the power of precision fermentation to create a proprietary flavoring ingredient. Founder Pat Brown and his team **determined** that heme protein from the root nodules of soy plants functions in plant-based meat as heme protein from animals functions in conventional meat, but they recognized that the ingredient could be produced at scale only using microbial fermentation. The successes of Quorn and Impossible Foods have led a massive wave of entrepreneurs to develop new products that expand upon the innovative use of fungi and other microbes to create tasty, healthful animal product analogs with broad appeal.

Despite the high activity level, the alternative protein industry is extremely young. The median founding year of the dedicated alternative protein companies is 2018, and the median founding year of companies with alternative protein business lines is 2012. Of the 44 identified companies devoted to this space (Table 2), all but Quorn formed after 2012, and 50% formed no earlier than 2016. In 2019 alone, 14 new companies formed. In the first half of 2020, another seven emerged.



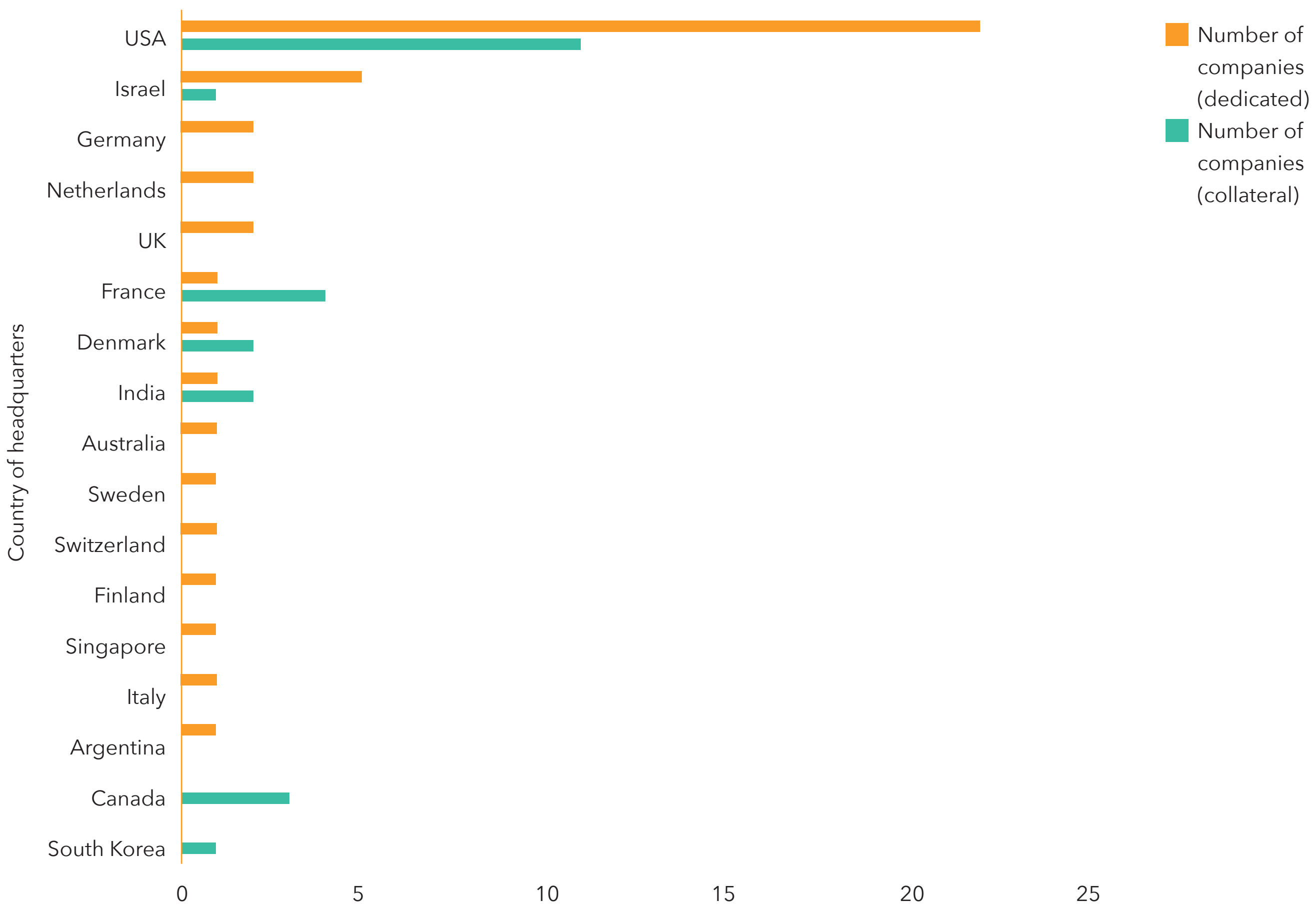
Source: GFI.

FIGURE 3. Number of dedicated alternative protein companies (2013–2020).

Source: Atlast Food Co.

Section 2: Companies

The field is growing not only in size but in geographic scope. Companies involved in fermentation for alternative protein applications span much of the globe. Companies dedicated to alternative protein applications operate in at least 16 countries: the United States, France, Denmark, Germany, India, Netherlands, United Kingdom, Canada, Australia, Sweden, Switzerland, Singapore, Finland, South Korea, Italy, and Israel (Figure 4). The largest concentration of companies is in the United States (22). Europe is home to 16 and Asia-Pacific five. Of the 20 companies formed in 2019 or 2020, 12 are outside the United States. Of the 24 identified companies working in fermentation for alternative proteins as a business line (Table 3), 11 are in the United States.



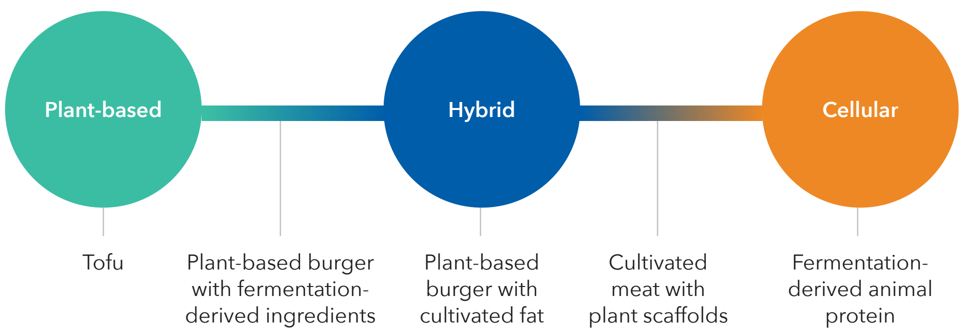
Source: GFI.

FIGURE 4. Geographic distribution of fermentation companies in alternative proteins.

Section 2: Companies

Looking ahead

The vast majority of fermentation-enabled alternative protein products either have come to market in the past few years or are likely to launch within the next few years. Many will not rely purely on fermentation but will include plant and animal cell components, just as Impossible Foods' beef derives from a mixture of plant and microbial sources. As elaborated on in the next sections, intersections of the three alternative protein categories will enable a new wave of paradigm-shifting meat, egg, and dairy products and ingredients that meet consumer expectations for taste, price, and accessibility.



As these products enter the market and demonstrate traction among consumers, industry activity is likely to accelerate. Many will not rely purely on fermentation but will include plant and animal cell components, just as Impossible Foods' beef derives from a mixture of plant and microbial sources. All this activity will improve the end products' taste and price, driving further adoption.

As discussed below, companies generally adopt a strategy that is primarily B2B or primarily B2C (business-to-consumer). Currently, about two-thirds of fermentation companies are pursuing B2B strategies. Most of these companies focus on serving B2C cultivated meat or plant-based meat, egg, or dairy companies, rather than other fermentation companies. We expect the category of B2B fermentation-company providers to grow as B2B cultivated-meat-company providers did in 2019, as highlighted in GFI's **state of the cultivated meat industry** report. The growth of these companies will lead to higher-quality, less expensive, more functional, and more diverse product formats. Further, as the alternative protein industry matures, we expect increased globalization of companies, particularly as more B2B opportunities emerge. Globalization will enable countries to leverage their comparative advantages, such as China's hardware manufacturing prowess for the creation of highly automated bioreactors and Brazil's large-scale agriculture for inexpensive fermentation feedstocks.

Section 3: Consumer-Facing Applications: End Products

Overview

Traditional fermentation has **long been used** to create delicious, nutrient-packed foods, such as cheese, yogurt, sauerkraut, miso, tempeh, and kimchi, as well as beer, wine, soy sauce, and kombucha. Its **earliest iterations** relied on native microbes from environmental sources, such as food ingredients, the air, or a cook's hands. However, humans have been cultivating specialized strains for centuries through adaptive selection. Now, culinarians and food manufacturers increasingly recognize the potential of more targeted use of fermentation to endow foods with unique flavor, texture, and nutritional attributes.

The customization of microbes for use in food production has been termed the "**second domestication**." The first wave of domestication, spanning many generations, leveraged selective breeding of animal and plant species for desirable traits, such as rapid growth and disease resistance, resulting in today's livestock and crops. The second wave presents an unprecedented opportunity to domesticate fungi, algae, bacteria, and other microbes to produce a fantastic variety of proteins and functional ingredients. Such domestication can be achieved more quickly and precisely than domestication of animals and plants because of microbes' much shorter life cycles and substantially greater variety, as well as technological advances in precision biology, screening and selection tools, and genomics. Pioneers of the second domestication include chef-scientists leveraging traditional fermentation, such as Danish chef René Redzepi, founder of Noma restaurant in Copenhagen

Mycelium-based chicken sandwich produced by Atlast Food Co. Source: Atlast Food Co.

(regarded as **one of the world's best restaurants**) and the Nordic Food Lab, focused largely on fermentation. Redzepi considers fermentation the "**future of cooking**" and incorporates it into **all Noma dishes**. In light of restaurant closures due to Covid-19, Noma launched a carryout **fermentation-enabled quinoa tempeh burger**, which customers are calling the best animal-free burger they've ever eaten. Other companies are also applying traditional fermentation in innovative ways, such as **Better Nature**, which makes animal-free meats from tempeh.

Advances in biotechnology, data analysis, and industrial design have enabled a much wider range of capabilities, allowing for expansion beyond traditional fermentation into precision and biomass fermentation. This increasingly precise biological control is establishing fermentation as an indispensable platform for innovations in both ingredients and primary protein production.

The past five years have seen unprecedented entrepreneurial efforts to commercialize fermentation-based solutions in the alternative protein industry. As early as 2015, these entrepreneurs secured top investors, such as SOSV, Horizons Ventures, and Techstars (in partnership with ZX Ventures, a subsidiary of AB InBev). Since then, IndieBio, a biotechnology accelerator and subsidiary of venture capital firm SOSV, has incubated fermentation-based companies New Culture, Prime Roots, Perfect Day, Clara Foods, Geltor, and NovoNutrients. Owing to the diversity of microbes and the flexibility they afford, these companies are delivering a broad swath of high-fidelity animal-free meat, egg, and dairy products, as well as new-to-the-world products.

Consumer product categories: Fermentation allows for a huge diversity of products

As many as **one trillion** species of microorganisms may exist on Earth. Compared with the few dozen animal species and several hundred plant species that humans routinely eat, microbes offer virtually endless opportunity to explore their food applications. This diversity of potential products and processes is further enhanced by the applicability of genetic editing and engineering to enable these microbes to manufacture specific animal and plant proteins, fats, and other molecules. Companies are using fermentation to produce ground meat products, whole-cut meats, eggs, milk, cheese, gelatin, seafood, fats, oils, pet food, and more. Fermentation is also enhancing plant-based products across all these categories.

Ground meat

Minced and ground meat were the first products in the recent wave of plant-based meat innovation (e.g., from **Beyond Meat** and **Impossible Foods**). Such semi-structured products lend themselves to improvement by traditional, biomass, and precision fermentation. **Quorn**, founded in 1985, was the first to use biomass fermentation to make ground meats. The company's patties, sausages, and minces emulate beef, chicken, and pork. Quorn uses a species of filamentous fungi, *Fusarium venenatum*, to produce their protein-rich products, which require 90% less energy and land than beef, according to the **company**. Quorn is no longer alone in this category. In June 2020, Sweden's Mycorena **soft-launched** their line of mycoprotein Swedish meatballs in local stores, and other companies are developing mycoprotein products. **More Foods** in Israel uses yeast as an alternative to plant-based proteins in meat products. Impossible Foods and Mediterranean Food Lab use precision and traditional fermentation, respectively, to create functional ingredients that dramatically improve the flavor and meatiness of products.

Outside tempeh and other fermented foods that are not intended to fully mimic the sensory properties of animal products, ground products make up the bulk of fermentation-enabled offerings widely available to consumers. However, products in the following formats are launching with increasing frequency—and innovative products in all other familiar formats are not far behind.

Source: Impossible Foods.

Whole-cut meats

For years, making restructured plant-based meat products, such as sausages, nuggets, and patties, has relied on low-moisture extrusion. New technologies have enabled plant-based meat producers to progress from these ground formats to pulled, shredded, and diced meats. **Twin-screw high-moisture extrusion** is the current stalwart for creating whole-muscle products that most resemble muscle strata. The past year has seen significant research into both new inputs (e.g., oilseed and pulses) and improving extrusion machinery, which is leading to better, more affordable structured meat products.

Fermentation also presents opportunities for enhanced texture and nutrition without extruders. Creating animal-free whole cuts and cutlets is a massive market opportunity, as whole-cut products (such as filets, bone-in products, and ham) are the **highest-margin and most desirable segment** of the **$1.7 trillion** global meat market. Colorado-based Meati has developed a line of whole-cut steak and chicken products. Meati uses submerged fermentation to mimic the muscular structure of meat. **Atlast Food Co.**, a spinout from mycelium innovation company **Ecovative**, uses solid-state fermentation to produce whole-cut meats. Bacon is their first product. Additionally, **Prime Roots** deploys mycoprotein to create a variety of innovative new products for direct-to-consumer sale. The company has also started with bacon, made from the filamentous fungus *Aspergillus oryzae* (also known as koji, the microbe used to produce miso). The 1000+ packages in their soft launch sold out **within hours**.

Submerged fermentation
Microbial cell culture in a vessel where cells are suspended in a liquid broth containing their nutrient feedstock. The equipment for performing submerged fermentation is akin to that found in breweries.

Solid-state fermentation
Microbial cells are seeded onto a moistened, solid feedstock and grown in an enclosed environment or an open-air environment. Tempeh production is an example of a solid-state fermentation process, where boiled and cooled soybeans serve as the solid feedstock.

Source: Atlast Food Co.

Meati's flagship steak. Source: Meati.

Section 3: Consumer-Facing Applications: End Products

Eggs and egg replacements

A small crop of companies has emerged to crack animal-free eggs by using fermentation to produce their functional components in a better way. **Fumi Ingredients** has developed an egg white replacement that acts as a foaming agent, heat-set gel, and emulsifier. **The Protein Brewery**, spun out of **BioScienz**, expresses the chicken ovalbumin gene (the most prevalent protein in egg whites) in a fungal host strain. Other companies have developed whole egg replacements, such as "**the egg**," a protist-derived powdered egg by **Noblegen** that launched in early 2020.

Company highlight: Clara Foods

Clara Foods, founded in 2014 by **New Harvest** fellows Arturo Elizondo and David Anchel, is the first fermentation-based egg protein company. The company uses yeast to produce egg albumen proteins (the major constituents of egg whites) as an ingredient for cooking and baking. In April 2019, Clara Foods **announced** a joint development and distribution partnership with global ingredient supplier Ingredion to fast-track the commercialization of the world's first animal-free egg proteins. Clara Foods has raised over $56 million in venture capital from top investors in the industry, including Ingredion, B37, Hemisphere Ventures, IndieBio (SOSV), Blue Horizon Ventures, and CPT Capital.

Clara Foods

Dairy: Milk, ice cream, butter, and cheese

One of the most promising applications for fermentation is dairy products. Most companies that have succeeded in making desirable plant-based cheese, such as **Treeline** and **Miyoko's**, have done so through nut-cream fermentation akin to traditional dairy cheese production. Other companies including **New Culture**, **Change Foods**, Cultivated, and **LegenDairy** recently emerged to create dairy proteins and fats that will usher in a wave of plant-based, fermentation-enabled dairy.

Company highlight: Perfect Day

Perfect Day, formed in 2014 by Isha Datar of New Harvest and New Harvest community members Ryan Pandya and Perumal Gandhi, is the first company to make real milk proteins—casein and whey—for food applications using microbes rather than mammary glands. This production technology will enable a new generation of biomimicking flora-based cheese, ice cream, yogurt, and butter. In late 2018, Perfect Day commercialized their ingredients through a joint development agreement with global agri-food company ADM. In early 2020, Perfect Day partnered with San Francisco ice cream producer Smitten to sell animal-free ice cream—the first such animal-free dairy ice cream on the market—on Smitten's local and regional direct-to-consumer platform. Also in 2020, Perfect Day spun out The Urgent Company, which started a new animal-free ice cream brand, Brave Robot. By the end of 2019, Perfect Day had raised over $200 million in venture capital from SOSV, Horizons Ventures, Temasek, Green Monday Ventures, Continental Grain Company, CPT Capital, ADM, and others. In July 2020, Perfect Day announced that their Series C round had expanded from $140 million to $300 million, led by a $50 million tranche from the Canada Pension Plan Investment Board. The company's total investment is now more than $360 million.

Brave Robot's animal-free ice cream made in partnership with Perfect Day. Source: Perfect Day.

Section 3: Consumer-Facing Applications: End Products

Gelatin

Gelatin is partially degraded collagen protein, traditionally derived from animal connective tissue as a byproduct of meat rendering. Because of its gelling properties, gelatin is used in a number of food applications and cosmetics. **Geltor**, the leader in the animal-free gelatin field, uses precision fermentation to produce their line of **collagen products**. Geltor's **go-to-market strategy** has been to enter higher-value, lower-volume markets—cosmetics, supplements, and life sciences—on their way to achieving the scale and prices required to compete with animal-sourced gelatin in food. While **multiple manufacturers** make recombinant collagen for research, tissue engineering, and cosmetic purposes, these conventional players have not expressed intention to move into food applications, and they typically produce only human collagen.

Source: Geltor.

Seafood

One of the least developed areas of alternative proteins is plant-based seafood. Fermentation, particularly with microalgae, may hold the key to unlocking this category. Quorn's **fishless fingers** are the only fermentation-enabled seafood products widely available. **Odontella**, for example, has launched a structured salmon analog using both seaweed and microalgae, but they are still in the process of commercializing their product. On June 8, 2020—World Oceans Day—Meati posted an Instagram **teaser**: a mycelium-based flaky fish in a basket of fish and chips. In July 2020, 3F Bio **announced** a prototype mycoprotein tuna steak produced via a 3-D printer made by Natural Machines. Several plant-based products, such as Gardein's frozen fish and crab cakes and Good Catch's tuna, make use of microalgal omega-3 oils as well. See GFI's white paper ***An Ocean of Opportunity*** to learn more about the potential of seafood alternatives.

Source: Air Protein.

Box 1: Microalgae may be having its moment

Omega-3 fatty acids, an important component of many types of fish oil, have long been used as a health supplement. Historically, these essential fatty acids have been produced through pulverizing fish, but they also exist in high amounts in some species of microalgae that can be grown through fermentation. This valuable potential market, in addition to microalgae as a source of **biofuel**, has led to scaled-up production and an optimized refinery process. Now, researchers and companies use microalgae as highly scalable biofactories for omega-3s and other helpful inputs for the alternative protein industry. **Odontella**, for example, uses microalgae (as well as **macroalgae**, such as kelp and seaweed) to produce a **line** of nutritious algae-based seafood, including salmon, tuna, caviar, prawns, and scallops. **Algama** has developed an **eggless mayonnaise** using microalgae. **Triton Algae Innovations** uses microalgae as an expression mechanism for their heme functional ingredient for plant-based meat. Many more companies have developed extremely efficient processes for cultivating microalgae, as well as new applications, such as additives, colorants, protein powders, and other ingredients. These companies, among others, are **Back of the Yards Algae Sciences**, **AlgaVia**, **FermentAlg**, **BioTork**, **Sophie's BioNutrients**, and **Spira**. Alternative proteins present a promising opportunity for microalgae because the total addressable market is much larger than that for omega-3s, and food is higher value than biofuels.

Fats and oils

Fats are key contributors to the sensory experience of eating meat, egg, and dairy products. Microbial fermentation produces a wide array of fats, including fats that are critical to either nutrition or functionality of animal products but challenging to source from the plant kingdom. The most notable on-market example is microalgae cultivation to produce algal omega-3 fatty acids, such as EPA and DHA, which are not produced by terrestrial plants. Companies such as Algarithm, DSM, iWi, and Corbion produce algal- or fungal-derived omega-3s. Several plant-based fish products, such as Good Catch's tuna, incorporate these fats for their characteristic fishy flavor and aroma, as well as nutritional benefits.

Because of limited global supply and the environmental impact of palm farming, interest in fermentation to produce animal fats and other saturated fats, such as palmitic acid (the dominant fatty acid in palm oil), is increasing. C16 Biosciences and Nourish Ingredients use microorganisms with altered lipid synthesis pathways to produce desirable fats. Also, Perfect Day and Motif FoodWorks have announced new initiatives for developing fat solutions for plant-based dairy and meat applications.

Section 3: Consumer-Facing Applications: End Products

Pet food

Pet food is a promising application for fermentation due to fermentation's ability to create proteins that are scarce in plants but desirable for vegan pet foods. Pet food is a large industry with great opportunity for impact. Pet food is not only a **$30 billion market** but the cause of about **25%–30% of the environmental impact of eating meat** in the United States. If U.S. dogs and cats were a country, they would be the world's fifth-largest in meat consumption. Additionally, human-food producers can leverage research and technology development for pet food applications.

Two startups have emerged as leaders in the use of fermentation for pet food. **Wild Earth**, founded in 2017 by IndieBio co-founder Ryan Bethencourt, **debuted** a high-protein dog food from yeast in 2019 after the company launched their prototype koji-based dog treat in 2018. **Bond Pet Food** takes a different approach, using microbes to produce specific animal muscle proteins. In March 2020, Bond **introduced** their first product: a high-protein dog treat produced with a novel strain of yeast.

Wild Earth CEO Ryan Bethencourt eating his yeast-based dog food. Source: Wild Earth.

Looking ahead

Fermentation is poised to become a major contributor to the alternative protein industry as consumers are drawn by the taste, texture, health benefits, and affordability that the technology imparts to a range of alternative protein products. Fermentation is likely to play an essential role in delivering the next wave of cultivated and plant-, algae-, and fungi-based foods—that meet or exceed the sensory and functional paradigms of their animal-based counterparts. In late 2019 and early 2020, a number of regional or online products launched, particularly cheese, ice cream, and meat. We expect these products to roll out nationally in the coming years and achieve great market success as consumers trial them. We have only just begun to explore end products enabled by fermentation.

Source: Meati.

Section 4: Business-Facing Applications: Ingredients

Incumbents play a critical role in enzyme solutions and scaling

Incumbents in the B2B fermentation industry include manufacturers of food processing enzymes, flavoring ingredients, vitamins, and live microorganisms for fermented foods such as cheese, yogurt, and preserved meat. These companies, which include Cargill, DuPont, AB Enzymes, Biocatalysts, Novozymes, Kerry, ADM, DSM, Amano, and Ajinomoto, have deep expertise in enzyme development, strain development, and large-scale manufacturing.

While the alternative protein industry is not a major fraction of their business, these companies recognize the growing importance of this new application area and are developing novel solutions accordingly. For example, DuPont—after making a **huge investment in plant-based meat** by merging with International Flavors and Fragrances Inc.—has launched a new line of **live microbial cultures** optimized for plant-based dairy products. This is part of their recent push to develop **comprehensive ingredient solutions** for the plant-based industry. Similarly, Novozymes has expanded their marketing of enzymes for improving **flavor and functionality** of plant proteins, and they have developed **tailored enzyme toolkits** to support product development around specific plant ingredients and product categories, such as oat-based drinks. DSM also recently launched a **portfolio of enzyme solutions** targeting plant-based dairy product developers.

Because of their massive fermentation capacity and deep expertise in large-scale production, these companies often perform contract manufacturing in addition to manufacturing their own products. Thus, they may be ideal candidates for scaling or joint venture partnerships with emerging fermentation companies targeting the alternative protein industry. For example, ADM and Perfect Day have entered a **joint development agreement** to scale animal-free dairy protein production. Such partnerships enable new players to leverage existing infrastructure and operational expertise to scale more quickly and cost-effectively than they would by building new facilities.

Section 4: Business-Facing Applications: Ingredients

Emerging B2B companies as suppliers and service providers for the alternative protein industry

The majority of B2B companies using fermentation for alternative protein products position themselves as ingredient suppliers that empower B2C companies to improve their branded products. Companies such as MycoTechnology and 3F Bio (see highlights below) produce natural microbe-derived flavoring solutions or bulk proteins for use in consumer-facing products, and companies such as Clara Foods, **Fybraworks Foods**, and Geltor leverage biotechnology to produce genuine animal proteins in microbial or mycelial hosts for such products. Scale, cost, and functionality are these companies' core drivers for differentiation and adding value to the alternative protein ecosystem.

Company highlight: MycoTechnology

MycoTechnology

Colorado-based MycoTechnology has demonstrated two distinct use cases for fermentation as an enabling technology platform for the plant-based sector. Their first product, ClearTaste™, is derived from an extract of fungal mycelium cultivation and serves as a flavor modulator. In the context of the alternative protein industry, its primary use is as a bitter blocker for undesirable off-flavors in some plant proteins. This product is an illuminating example of fermentation's potential to cater to consumer-led interest in so-called clean label products. Many existing flavor modulators are derived through synthetic chemistry, so this paradigm of screening natural compounds from fermented organisms to identify natural products that perform the same flavor modulatory function offers a route to clean label products without sacrificing taste.

MycoTechnology's second product, PureTaste™, uses shiitake mycelium fermentation of a pea and rice protein feedstock to improve the flavor, aroma, and functional properties of the feedstock. This approach illustrates one of the first applications of the most powerful historical role of fungi in food: as bioconverters of foodstuffs into more flavorful, nutritious, and functional forms to address key challenges specific to the plant protein sector. Specifically, the pea- and rice-plant feedstock fermented with PureTaste™ exhibits reduced undesirable odor and flavor, greater water and oil binding capacity, and improved capacity for texturization relative to the unfermented raw materials. **Planterra**, a subsidiary of the world's largest meat company, JBS, uses PureTaste™ to produce their new Ozo brand line of plant-based meats.

Company highlight: 3F Bio

Scotland-based 3F Bio provides an example of innovation in feedstock use and industrial processes to derive new value from an existing fungal strain. The company uses the same filamentous fungal species used for decades by mycoprotein company Quorn, but they position themselves as a B2B supplier of Abunda™, their fungal protein. 3F Bio's approach is to improve both sustainability and cost by co-locating their production facilities with bioethanol production plants, thus creating an "integrated biorefinery" that is able to leverage all side streams of the input biomass on-site.

The feedstock for 3F Bio's mycoprotein fermentation is the residual biomass of bioethanol fermentation of grains, such as corn and wheat. Currently, the vast majority of these leftovers are sold to the animal feed industry as a low-cost source of protein and calories. 3F Bio's fungal strain can convert this low-quality, minimally digestible biomaterial into a much higher quality, more palatable ingredient for use in a variety of meat alternative products. In July 2019, 3F Bio and nearly a dozen partners, including cultivated meat company Mosa Meats and plant-based meat brand Vivera, **announced a partnership** to build the first such commercial-scale integrated biorefinery.

3FBIO

An additional layer of B2B activity exists in the fermentation sector: companies positioning themselves as service providers and technology development partners for B2B or B2C fermentation companies. **Culture Biosciences** is an example of a process optimization service provider that has supported many fermentation companies, including Geltor, Clara Foods, Modern Meadow, and C16 Biosciences, to accelerate their process development and cost curve progression while reducing their capital expenditure for in-house R&D.

Section 4: Business-Facing Applications: Ingredients

Company highlight: Motif FoodWorks

Motif FoodWorks is a striking example of leveraging technology platforms originally pioneered for parallel industries (e.g., industrial biotechnology, therapeutics, and even biomaterials) to advance the alternative protein industry.

In February 2019, synthetic biology leader Ginkgo Bioworks **announced the spin out** of Motif—seeded with $90 million. Motif was specifically created to expand the capabilities of Ginkgo's biological foundry toward applications in meat, egg, and dairy replacements. Ginkgo serves as a technology development partner for strain and biosynthetic pathway development, while Motif is tasked with identifying target molecules and manufacturing them as flavoring and functionality solutions for the plant-based sector. By August 2019, Motif had secured an additional $27 million in funding, with plans to launch their first B2B commercial products in **early 2021**.

In addition to their recent focus on fat solutions, Motif has **established a partnership** with researchers at the University of Queensland in Australia to develop high-throughput methods for assessing texture, which is currently handled by expensive, variable, and time-intensive sensory expert panels. These new automated screening methods, coupled with Motif's expansive pipeline of host strain and protein expression optimization tools, will enable rapid iteration of protein design and selection to develop ingredients that improve the quality of plant-based meat, egg, and dairy products.

Looking ahead

As activity within fermentation for alternative protein applications grows, we expect an increased number of both established and emerging companies to target fermentation businesses as their core clientele. Continued growth of this technology, as well as optimization of the ecosystem, will dramatically accelerate the rate at which new companies bring fermentation-enabled alternative protein ingredients and products to market. In coming years, we also anticipate a more active and visible role for contract manufacturing as incumbent fermentation companies pivot from low-value ingredients, such as amino acids used predominantly in animal feed, toward higher-value fermentation-derived ingredients for the alternative protein industry.

Mycelium-based chicken shawarma from Atlast Food Co. Source: Atlast Food Co.

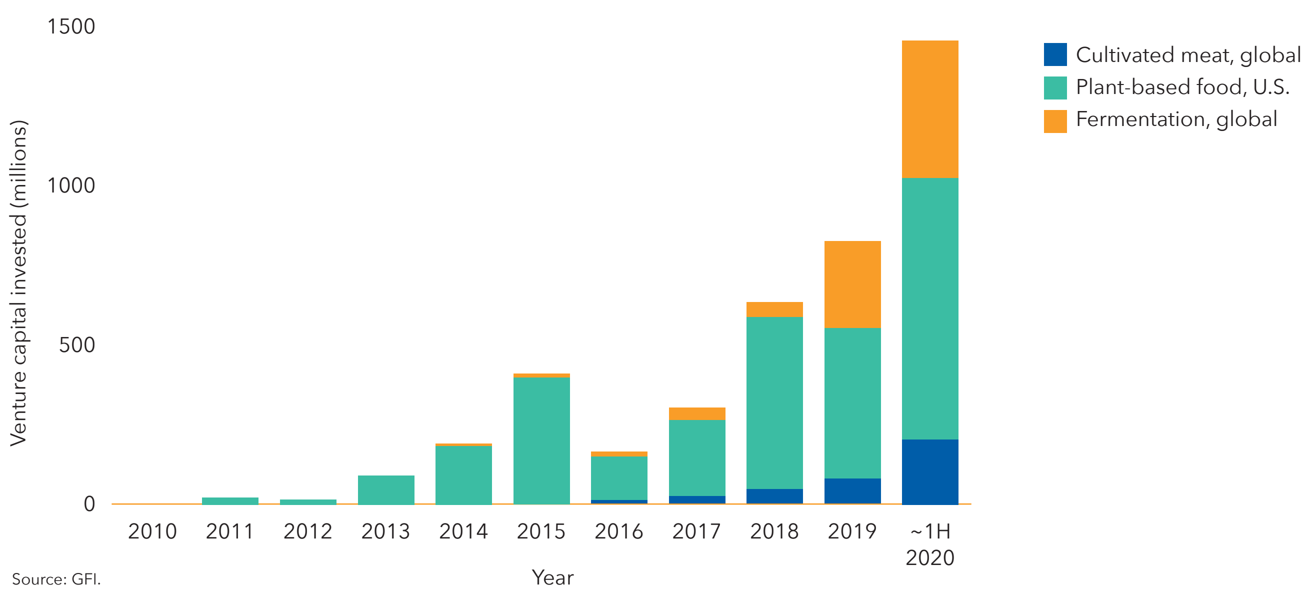
Section 5: Investments

Overview

The fermentation-enabled alternative protein subsector goes back as far as 1985, when Quorn became the first commercial player in the space. Despite Quorn's retail sales achievements in the subsector (among the top 10 in the **United States** and number one in the **United Kingdom** in 2019) and financial success (sold to Monde Nissin for more than $725 million in 2015), venture capital investment in fermentation for alternative protein applications was minimal until 2013.

That year, Triton Algae Innovations became the first company producing or enabling animal-free formulations through fermentation to receive outside venture capital: a $5 million investment from Heliae Development. Since then, fermentation companies devoted to alternative proteins have raised more than $837 million in venture capital funding; of this, $274 million closed in 2019, and $435 million closed in the first seven months of 2020 alone (Figure 7).

Although yearly global venture capital investment in fermentation companies did not surpass $10 million dollars until 2015, fermentation has quickly become a robust part of the investment landscape in alternative proteins. For example, in 2019, fermentation companies raised over 3.5 times more capital than all cultivated meat companies and close to 60% as much as plant-based food companies based or selling in the United States that year. Fundraising rounds—all exceeding $20 million—for Perfect Day, Motif FoodWorks, Clara Foods, Nature's Fynd, and MycoTechnology drove this large capital influx in 2019. In 2020, investment in fermentation accelerated to the highest level ever.



Source: GFI.

FIGURE 5. Venture capital investment trends in alternative proteins (2010–July 15, 2020).

Section 5: Investments

Box 2: Data collection methodology
In calculating investment figures for this report, we used our **company database** to create a custom list of 24 companies that appear to be solely or primarily focused on fermentation for alternative protein applications (listed in Table 1) in PitchBook: 3F Bio, Afineur, AlgaVia, Atlast Food Co., Biorealize, Bond Pet Foods, Clara Foods, FUMI Ingredients, Kinoko-Tech, LegenDairy Foods, Meati, Motif FoodWorks, Mushlabs, Mycorena, MycoTechnology, Nature's Fynd, New Culture, Perfect Day, Prime Roots, Provenance Bio, Quorn Foods, Solar Foods, The Protein Brewery, Triton Algae Innovations, and Wild Earth. According to inclusion criteria, we excluded at least 26 companies working in the space but whose investment may not flow primarily to alternative protein applications, such as Geltor, which has raised more than $117 million and also works in cosmetics. "Investment activity" in this section includes venture capital, mergers, acquisitions, and buyouts but not secondary transactions, non-convertible debt, or grants. Investments are further divided into "venture capital" (angel funding, seed funding, crowdfunding, early-stage venture capital, late-stage venture capital, accelerator or incubator funding, private equity growth/expansion, capitalization, corporate venture, and convertible debt) and "exits" (mergers, acquisitions, IPOs, subsequent share offerings, and buyouts). The investment figures herein represent a substantial underestimate because they exclude corporate R&D investment, academic investment, and deals not disclosed or available on PitchBook.

Deals

66
(2013-July 15, 2020)
21
in 2019
14
in 2020 (through July 15)

Venture capital

$837 million
(2013–July 15, 2020)
$140 million
(largest round 2019)
$274 million
(raised in 2019)
$435 million
(raised in ~first half of 2020)
85%
of all-time funding raised in 2019 and ~1H 2020

Unique investors

180
19 countries

Exits

$1.49 billion
(Quorn)

FIGURE 6. Fermentation investment overview.

See Box 2 for GFI's data collection methodology and definitions of "investments," "venture capital," and "exits."

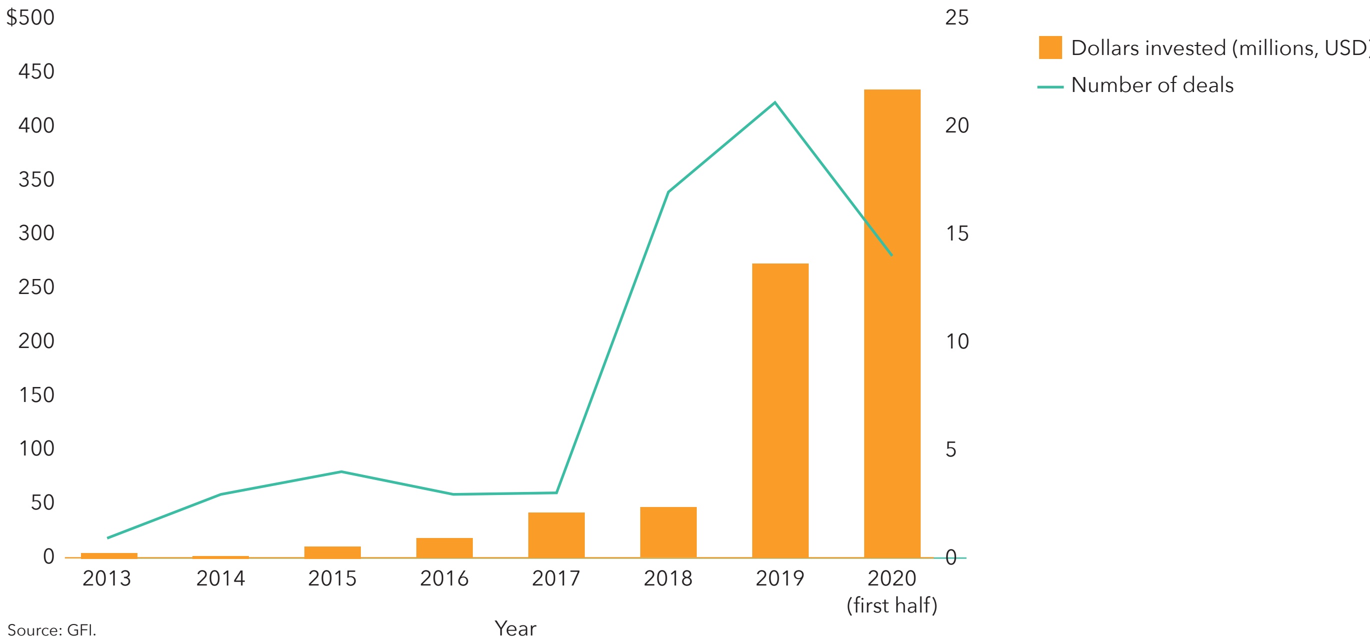
Section 5: Investments

Venture capital investments

Investment in fermentation innovation reached new heights in 2019; fifteen companies raised venture capital investments in 21 separate deals, ranging from seed to Series C (Figure 7). This means that about 68% of all industry venture capital investment through the end of 2019 occurred in the prior 12 months. Even amid the Covid-19 pandemic, venture capital funding in the first half of 2020 surpassed all other years combined. From January 1, 2020, to July 15, 2020, fermentation companies brought in $435.38 million in venture funding across 14 deals and nine companies. Deals include the largest venture capital fundraising round in the sector's history, a $300 million Series C **round** raised by Perfect Day to scale up animal-free dairy production and expand their B2B partner portfolio. The Series C was initially announced in October 2019 as a $140 million investment led by Temasek Holdings (a sovereign wealth fund of Singapore and prolific venture capital fund). This fundraising round partially closed in December 2019, but in July 2020 the Series C—led by Canada's largest pension fund—expanded by $160 million dollars, bringing it to $300 million and total investment in the company to $360 million. We categorize the full Series C as closing in July 2020.

Section 5: Investments

This Series C brings total venture capital investment in the sector to $837.25 million and means that 52% of all venture funding raised by fermentation companies closed in roughly the first half of 2020. 2019 and the first half of 2020 combined for 85% of all venture capital raised by the sector. Investment is expected to further increase as companies mature, demonstrate proof of concept, and scale alongside the rest of the alternative protein industry.



Source: GFI.

FIGURE 7. Total venture capital invested in fermentation companies (2013–July 15, 2020).

Section 5: Investments

TABLE 4. Top 10 most funded fermentation companies

This table provides an overview of venture capital fundraising by alternative protein fermentation companies. The list features only those companies with data in GFI's custom PitchBook list of 24 qualified companies—focused primarily on alternative protein production for human or pet food through microbial fermentation (Table 1). It does not include the >50 companies that do serious work in fermentation innovation for alternative proteins but maintain their primary focus on other use cases for fermentation, such as chemical production or aquaculture feed.

Company	Location	Largest round (date)	Total amount raised (round)	Institutional investors
Perfect Day	San Francisco, CA, USA	$300 million (Jul. 2020)	$361.48 million (Series C)	Canada Pension Plan Investment Board, SOSV, Horizons Ventures, B37 Ventures, CPT Capital, Green Monday Ventures, ICONIC Capital, Lion Ventures, Temasek Holdings, Verus International, ADM Capital
MycoTechnology	Aurora, CO, USA	$39 million (Jun. 2020)	$120.67 million (Series D)	Closed Loop Capital, Kinetic Ventures, Middleland Capital, S2G Ventures, Seventure Partners, Wavemaker Partners, Ajinomoto, Bunge, Continental Grain Company, eighteen94 capital, Emerson Collective, GreatPoint Ventures, Tao Capital Partners, Windy City, ADM Capital, DNS-Hiitake, Kellogg Capital Group, TML-Invest, Tyson Ventures, Evolution VC Partners, Kingdom Capital Group, Greenleaf Foods, SPC, Rich Products Ventures
Motif FoodWorks	Boston, MA, USA	$90 million (Feb. 2019)	$117.50 million (Series A)	Breakthrough Energy Ventures, CPT Capital, Fonterra Ventures, General Atlantic, Louis Dreyfus Company, Viking Global Investors, Anchorage Capital Group, The Yard Ventures
Nature's Fynd	Chicago, IL, USA	$80 million (Mar. 2020)	$113 million (Series B)	1955 Capital, ADM Ventures, Breakthrough Energy Ventures, Danone Manifesto Ventures, Lauder Partners, Liebelson family office, Generation Investment Management, Mousse Partners
Clara Foods	San Francisco, CA, USA	$40 million (Apr. 2019)	$56.80 million (Series B)	SOSV, UpHonest Capital, Wei Guo, B37 Ventures, Blue Horizon Ventures, Starlight Ventures, VegInvest, B37 Ventures, Beyond Investing, CPT Capital, Hemisphere Ventures, Ingredion, IOVC, Main Sequence Ventures, MicroVentures, Veronorte

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Wild Earth	Berkeley, CA, USA	$11 million (May 2019)	$15.55 million (Series A)	BABEL Ventures, Blue Horizon Corporation, Civilization Ventures, Felicis Ventures, Social Impact Capital, Stray Dog Capital, VegInvest, Aera VC, Everhope Capital, Founders Fund, M Ventures, Thiel Capital, Vectr Ventures
3F Bio	Glasgow, Scotland, UK	$8.63 million (Apr. 2018)	$9.22 million (Series A)	Data Collective, EOS Technology Investment Syndicate, Scottish Enterprise, University of Strathclyde Endowment, CPT Capital
Meati	Boulder, CO, USA	$3.2 million (Jun. 2020)	$8.00 million (seed)	Cleantech Open Midwest, Mid-West Energy Research Consortium, Chain Reaction Innovations, Better Ventures, Bluestein & Associates, Congruent Ventures, Fifty Years, Prelude Ventures, Social Starts, The March Fund, Trust Ventures, Unovis Partners, Boulder Food Group
Atlast Food Co.	Green Island, NY, USA	$7 million (May 2020)	$7 million (seed)	Alpha Impact Investment Management, Stray Dog Capital, Unovis Partners
Triton Algae Innovations	San Diego, CA, USA	$5 million (Sept. 2013)	$5 million (seed)	Heliae Development

Exits: Quorn leads the pack

The alternative protein fermentation sector is too young to expect many "exits," the liquidity events such as initial public offerings or acquisitions that drive the venture capital investment model. However, Quorn, the mycoprotein pioneer founded decades before most other mycoprotein companies, provides a promising case study. Rank Hovis McDougall (RHM), a UK-based food company, began research and the regulatory approval process for their products in the 1960s. However, not until 1985 was the brand "Quorn" (named after a British village) first marketed via a joint venture between RHM and Imperial Chemical Industries (ICI).

Quorn first sold at Sainsbury's in the United Kingdom in the form of savory pies. Other parts of Europe followed and finally North America in 2002. As one of the first market entrants in alternative proteins, Quorn enjoyed market dominance and commercial success. In 1993, Quorn was spun off ICI, which had acquired all of RHM's shares, to AstraZeneca. In 2003, Montagu Private Equity bought Quorn for $116 million before selling it two years later to Premier Foods for $315 million. In 2011, other private equity investors acquired Quorn before Monde Nissin, a Philippines-based food company, ultimately acquired it for $726 million in 2017. Notably, Quorn has also successfully secured large tranches of debt financing, including a $147 million debt facility from CitiGroup Global Markets and HSBC Bank in March 2019 per PitchBook. We expect other fermentation company exits within years, not decades.

Section 5: Investments

Investors

According to PitchBook, fermentation companies have drawn funding from at least 180 unique investors. For comparison, agtech companies have secured more than 5,800 investors and foodtech companies over 3,500 per PitchBook. Although a small field of investors—natural for a nascent industry—it includes incredible visionary and strategic companies and individuals. Notable investors span large corporations, top accelerators, food conglomerates, governments, prolific venture capital investors, impact investors, and specialized alternative protein funds. They include Louis Dreyfus Co., Bunge Ventures, Kellogg Capital, ADM Capital, Danone Manifesto Ventures, Kraft Heinz Evolv Ventures, Continental Grain Company, Mars, Tyson Ventures, SOSV (IndieBio), Viking Global Investors, Thiel Capital, Breakthrough Energy Ventures, Fifty Years, Generation Investment Management, Mayfield Fund, Techstars, and specialists New Crop Capital, Blue Horizon Ventures, CPT Capital, Purple Orange Ventures, and Stray Dog Capital.

Total investors in fermentation companies span 19 countries across five continents. Half these investors—98 total—are headquartered in the United States. The next largest concentration of investors is in Europe, with 63 investors across 12 countries. The United Kingdom boasts 17 investors followed by Sweden with 10, France with eight, Netherlands with seven, and Finland with six. Unique investors across Asia total 13, with eight in China; two in Singapore; and one in India, the Philippines, and Japan. Australia, New Zealand, the United Arab Emirates, Barbados, and Colombia combined host six investors.

Section 5: Investments

TABLE 5. Investors in alternative protein fermentation companies by deal count

The following table lists investors in fermentation companies, filtered by the number of investments. Only those investors with at least two investments, per PitchBook, are included.[1]

Investor	Number of investments (including follow on investments)	Number of individual portfolio companies	Primary investor type	HQ location
SOSV	12	6	Venture capital	Princeton, NJ
CPT Capital	10	7	Venture capital	London, United Kingdom
Horizons Ventures	5	1	Venture capital	Hong Kong
B37 Ventures	3	2	Venture capital	San Francisco, CA
Breakthrough Energy Ventures	3	2	Venture capital	Kirkland, WA
Continental Grain Company	3	2	Corporation	New York, NY
Middleland Capital	3	1	Venture capital	Washington, DC
S2G Ventures	3	1	Venture capital	Chicago, IL
Temasek Holdings	3	1	Sovereign wealth fund	Singapore
VegInvest	3	2	Venture capital	New York, NY
1955 Capital	2	1	Venture capital	Los Altos, CA
ADM Capital	2	2	Hedge fund	Hong Kong
Archer Daniels Midland Ventures	2	1	Corporate venture capital	St. Louis, MO
Agronomics (LON: ANIC)	2	2	Venture capital	Douglas, United Kingdom
Atlantic Food Labs	2	2	Venture capital	Berlin, Germany
Bånt AB	2	1	Venture capital	Luleå, Sweden
Closed Loop Capital	2	1	Venture capital	Radnor, PA
Danone Manifesto Ventures	2	1	Corporate venture capital	New York, NY
Data Collective	2	1	Venture capital	Palo Alto, CA
eighteen94 capital	2	1	Corporate venture capital	Battle Creek, MI
EOS Technology Investment Syndicate	2	1	Angel group	Saint Andrews, United Kingdom
Felicis Ventures	2	1	Venture capital	Menlo Park, CA
Founders Fund	2	1	Venture capital	San Francisco, CA
General Atlantic	2	1	Growth/expansion	New York, NY
Kale United	2	1	Venture capital	Stockholm, Sweden

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Lever VC	2	1	Venture capital	Brooklyn, NY
National Science Foundation	2	2	Government	Alexandria, VA
Plantbase Foundation	2	1	Corporation	Heemstede, Netherlands
ProVeg Incubator	2	2	Accelerator/incubator	Berlin, Germany
Scottish Enterprise	2	1	Venture capital	Glasgow, United Kingdom
Seventure Partners	2	1	Venture capital	Paris, France
Social Starts	2	2	Venture capital	San Francisco, CA
University of Strathclyde Endowment	2	1	Limited partner	Glasgow, United Kingdom
Unovis Partners	2	2	Venture capital	New York, NY
Vectr Ventures	2	1	Venture capital	Hong Kong

Source: GFI analysis of PitchBook data.

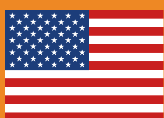
1. Investors with a single investment in alternative protein fermentation companies include the following: 100 Plus Capital, Aera VC, Agoranov, Ajinomoto (TKS: 2802), Ali Partovi, Alumni Ventures Group, Amadori, Anchorage Capital Group, Andante Asset Management, Angelor Capitale, AstraZeneca (LON: AZN), Atomico, BABEL Ventures, Bee Partners, Bertebos Foundation, Better Ventures, Beyond Investing, Bitburger Ventures, Bits x Bites, Blu1887, Blue Horizon Ventures, Bluestein & Associates, Boost VC, Brad Feld, Bunge Ventures (NYS: BG), Chain Reaction Innovations, Chalmers Innovation Office, Civilization Ventures, Cleantech Open Midwest, Collaborative Fund, Congruent Ventures, David Friedberg, David Larrabee, DNS-Hiitake, DreamIt Ventures, EIT Climate-KIC, EIT Food, Emerson Collective, Ephraim Lindenbaum, Eric McCarthey, European Commission, European Union, Everhope Capital, Evolution VC Partners, Evolv Ventures, Exponent Private Equity, Falkenbergs Sparbanks Foundation, Fazer Group, FBG Invest, Fifty Years, Fonterra Ventures, FoodTech Accelerator, For Good Ventures, Generation Investment Management, GETIC, Ginkgo, GreatPoint Ventures, Green Campus Innovations, Greenleaf Foods, Green Monday Ventures, Groth & Co., GU Ventures, Hadi Partovi, Happiness Capital, Heliae Development, Hemisphere Ventures, Hexagon (STO: HEXA B), Holdix, ICONIQ Capital, Ilias Hicham, Ilya Kuntsevich, IndieBio, Ingredion (NYS: INGR), Innovation Industries (Amsterdam), Intermediate Capital Group (LON: ICP), IOVC, Jacques-Antoine Granjon, KBW Ventures, Kellogg Capital Group, Kinetic Ventures, Kingdom Capital Group, Lauder Partners, LES Foundation, Liebelson family office, Lifeline Ventures, Lion Ventures, Lisa Gansky, Louis Dreyfus Company, M Ventures, Main Sequence Ventures, Marc Simoncini, Mars, Mayfield Fund, MBC BioLabs, MicroVentures, Mid-West Energy Research Consortium, Monde Nissin, Montagu Private Equity, Mousse Partners, Nationale Postcode Loterij, Nick Elmslie, Paris&Co Incubateurs, Paul Grossinger, Plug and Play Tech Center, Prelude Ventures, Premier Foods (LON: PFD), Purple Orange Ventures, Radical Investments, Rich Products Ventures, Right Side Capital Management, Scott Banister, SHIFT Invest, Social Impact Capital, Sonny Vu, Starlight Ventures, StartLife, Stray Dog Capital, Tao Capital Partners, Techstars, The March Fund, The Yard Ventures, Thiel Capital, TML-Invest, True Ventures, Trust Ventures, Tyson Ventures, U.S. Environmental Protection Agency, United Business Media, United States Department of Agriculture, UpHonest Capital, Urban-X, Veronorte, Verus International, Viking Global Investors, Vinnova, VTT Ventures, Wavemaker Partners, Wei Guo, Windy City, Xavier Niel, Yield Lab, ZX Ventures, and Voima Ventures.

Section 5: Investments

Box 3: Government grants incubate an emerging industry

Fermentation is a paradigm-changing innovation. It can unlock new high-value uses for low-value agro-industrial byproducts, affordably nourish the world's growing population, and help ensure protein sovereignty and security (unlike slaughterhouse closures during a pandemic). Thus, it is not surprising that some governments have taken an active hand in supporting companies in the space.

The United States, the European Union, and Israel are among the first governments to provide support for the sector.



In the United States, at least three federal agencies have provided either grants or direct investments to fermentation companies working in alternative proteins. Nature's Fynd, for example, received $1.27 million in grants from the U.S. Environmental Protection Agency, National Science Foundation (NSF), and U.S. Department of Agriculture in 2014 and 2015. Meati (formerly Emergy Foods) also received a grant from NSF—$220,000 in 2019. Some government entities have made equity investments, such as the U.S. Department of Energy's investment in Meati, through the **incubator arm** of Argonne National Laboratory.

In early 2020, Mycorena received a 50,000-euro grant from the European Commission, the executive branch of the European Union. In 2019, 3F Bio received an investment from **EIT Food**, the EU food innovation incubator. Further, 3F Bio, alongside a consortium of other companies, received a 17-million-euro grant from the EU Horizon 2020 program to develop a zero-waste biorefinery to produce food-grade protein from low-cost, sustainable feedstocks. The project, called **PLENITUDE**, brings together 3F Bio, a bioethanol biorefinery, Bridge 2 Food, Mosa Meat (a cultivated meat company), Wageningen University, International Flavors & Fragrances, Alcogroup SA, and others. In June 2020, EIT Food Accelerator Network announced their 2020 **cohort**, which included Mycorena, as well as several cultivated meat and plant-based meat, egg, and dairy companies.

Announced in late 2019, the **EU Smart Protein project** is an initiative to **support the alternative protein industry** for a future-proof, sustainable, and nutritious food supply chain. It includes support for fermentation (fungi and side stream conversion) and has a total budget of about $10.5 million. The project includes a consortium of more than 30 industry partners, such as AB InBev. The European Union also administers the **ProFuture** program, a government-funded program promoting the production and use of microalgae in food and feed.

In Israel, home to the second-largest concentration of fermentation startups, companies **leverage** several robust incubator programs supported by the Israeli Innovation Authority, such as the **Kitchen FoodTech Hub**.

These investments are promising yet relatively small and from only a few governments. For perspective, total global private R&D investment in all alternative proteins is around $1 billion, whereas government investment in renewable energy in 2011 alone was more than **$8 billion**.

Looking ahead

Fermentation in the alternative protein industry presents an opportunity to fundamentally change the way the world eats. Companies have developed promising fermentation technology but are nascent, underresourced, and few. **Scaling up bioprocesses** from pilot to demonstration to full commercial, as well as developing additional use cases and optimizing this technology (see Section 6), will take billions of dollars in financing and R&D funding.

Despite the massive need for increased competition, funding, research, and infrastructure, we are optimistic. We expect to see not only additional venture capital invested in this space—from biotechnology investors, alternative protein investors, agrifoodtech investors, and mainstream funders—but more debt financing options to build production capacity in the coming years as these companies mature from seed and Series A rounds to Series B rounds and beyond. Further, GFI will continue to support this sector through our **competitive research grant program** (e.g., the current **oat fermentation** and **flavor base development** grants) and by advocating **increased government funding**.

Source: Air Protein.

Section 6: Science and Technology Opportunities

Overview

Despite microbial fermentation's long history in food and industrial biotechnology, tremendous potential for innovation remains untapped. The vast biological diversity of microbial species, coupled with virtually limitless biological synthesis capabilities, translates to immense opportunity for novel alternative protein solutions to emerge from fermentation-based approaches. Opportunities for advancing fermentation can be segmented into five key areas spanning the value chain: target selection and design, strain development, feedstock optimization, bioprocess design, and end-product formulation and manufacturing.

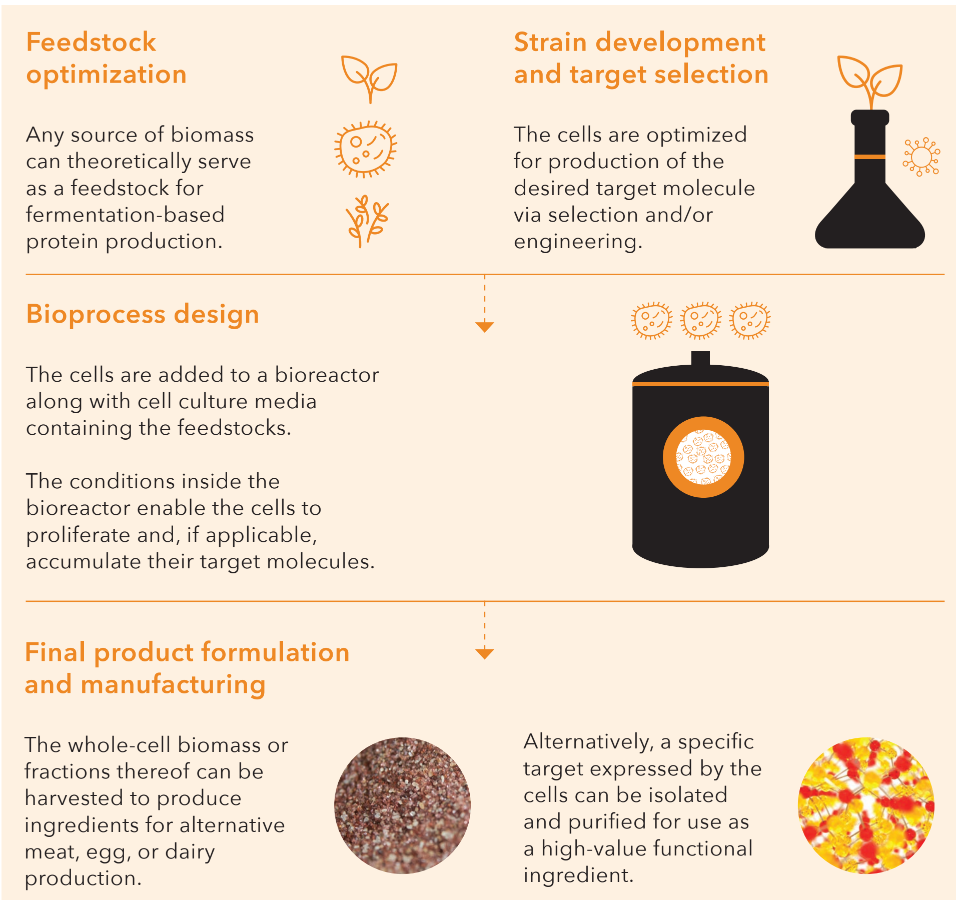


FIGURE 8. Opportunities exist for technology development across all aspects of the fermentation value chain.

Section 6: Science and Technology Opportunities

Key areas for science and technology development

Target selection and design

The concept of target selection and design applies only to precision fermentation. The molecule or molecules of interest are referred to as the target. The target can be a protein, a lipid, a flavor compound, a fragrance, an enzyme, a growth factor, a pigment, or another class of molecule.

In the case of a protein target, the instruction manual for synthesizing the target is encoded in the host organism's DNA, either as a naturally occurring gene or as a gene introduced through engineering. The first widely commercialized food ingredient produced through precision fermentation was recombinant chymosin. A coagulating enzyme used in cheese production, chymosin was formerly extracted from calves' stomachs. Most modern cheese production already uses this product of precision fermentation.

Because this milk-digesting enzyme exists naturally in calf stomachs, it is an animal protein that must be introduced into a microbial host to be produced through fermentation. But other proteins may be introduced through engineering or be native to various microbial strains. For example, the soy leghemoglobin protein produced by Impossible Foods is engineered into a yeast host strain for efficient, scalable production, while microalgae company Triton Algae Innovations is commercializing heme proteins that are native to their algal strains, so no engineering is involved.

Synthesis of non-protein targets cannot be encoded in the host's DNA. Instead, the genome encodes a series of enzymes that compose the biosynthetic pathway for producing the target molecules. For example, the target molecules for algal omega-3 production are the fatty acids DHA and EPA, but the instruction manual for manufacturing these fatty acids consists of several gene-encoding enzymes that convert precursor fatty acids into these desirable fatty acids within the cell.

Fermentation allows for a decoupling of a target molecule and its original mechanism of production. This decoupling vastly expands the search landscape for biomolecules with unique and valuable functions. First, ideal targets may originate in species that are extraordinarily rare, difficult to harvest, expensive, or otherwise inaccessible or impractical. Fermentation provides a mechanism for manufacturing these molecules at scales and prices suitable for commercial viability. Second, targets are not limited to those found in nature: Novel variants of target molecules can be engineered through random alteration and screening (directed evolution) or through rational design, leading to targets that exceed the performance of any naturally occurring version.

Target
The specific molecule or mixture of molecules being produced via precision fermentation. This can be a protein; a fat; or any molecule or compound that is producible through a biological pathway, such as a pigment, a vitamin, a flavoring, or an aroma.

Biosynthetic pathway
A series of chemical reactions that occurs within a cell to produce a molecule. While some steps in a biosynthetic pathway may occur spontaneously through chemistry alone, many steps are performed by an enzyme. These enzymes can be introduced into a host cell to equip that cell with the ability to make a new target molecule.

DHA and EPA
Docosahexaenoic acid and eicosapentaenoic acid are fatty acids within the omega-3 family that are typically associated with fish oil but can be produced by algae as well. DHA and EPA are long-chain omega-3 fatty acids (containing 22 and 20 carbon atoms, respectively), which can be produced from shorter-chain omega-3 fatty acids that are abundant in plant oils using enzymes that add extra carbon units to the chain. This reaction actually occurs within human cells but at low efficiencies.

Directed evolution
The process of selecting variants of a molecule that have evolved to exhibit a desired set of traits. The underlying concept is identical to artificial selection applied in the breeding of plants and animals during domestication but applied at the molecular level rather than to the organism as a whole.

Rational design
The process of designing a new molecule based on a deep understanding of the properties of related molecules. This technique requires some degree of predictive capability and insight into the mechanism by which a molecule's structure relates to its function.

Geltor's collagen production platform illustrates both aspects of this expanded search landscape. Gelatin from conventional animal sources is limited to a few species (predominantly pig and cow, although fish gelatin is also commercially available) that are processed in large quantities. But collagen is ubiquitous in the animal kingdom, and Geltor can manufacture collagen proteins from any species, including extinct species. In 2018, the company showcased the versatility of their platform with an animal-free leather book binding made from **jellyfish collagen** and gummy snacks made with **mastodon collagen**. Geltor also makes bespoke versions of collagen that are precisely tuned to the characteristics desired for a particular application—for example, gelatin that exhibits a specific gelling viscosity, elasticity, or melt temperature.

Similarly, fermentation allows for enzymes to be adapted or engineered to exhibit higher activity, novel substrate specificity, greater stability, or robustness under specific processing conditions, with dramatic implications for cost reduction. Such enzymes serve many purposes across the alternative protein industry. Fermentation holds immense potential to screen for natural variants of targets and to design new variants for augmented sensory, functional, or nutritional properties or for attributes that reduce costs and streamline manufacturing processes.

Strain development

Strain development accounts for a significant fraction of research in the fermentation sector thus far, but we have barely scratched the surface of possibility. High-throughput methods of strain selection, adaptation, screening, and engineering enable innovators to iterate new strains with greater speed and precision. They can select for more nuanced attributes, such as precise flavor-enhancing metabolite profiles, rather than simple traits, such as growth rates or temperature tolerance. While some of the strain development work in this sector is likely to involve biotechnological tools, such as gene editing and genetic engineering, vast progress remains to be made through simple adaptation and breeding strategies powered by advanced genomic insights.

Renewed interest in the concept of "single-cell protein," a term commonly used to refer to microbial whole-cell biomass, and the emergence of high-throughput screening and characterization tools merit a recanvassing of all known microbial species for their potential suitability as protein sources. Use of *Fusarium venenatum*, the filamentous fungus first commercialized by Quorn, emerged from precisely such a project. This particular search was initiated in the 1960s over concerns about an impending protein shortage, but the

Enzymatic activity
A measure of the rate at which an enzyme can catalyze a specific chemical reaction. Higher activity translates to faster reaction times, so less enzyme is required—translating to cost savings.

Substrate specificity
A reflection of the degree to which an enzyme performs only a single desired chemical reaction, converting one molecule (the substrate) to another. Some enzymes exhibit high specificity with very low off-target activity, while other, so-called promiscuous enzymes can accept multiple related substrates and may produce a range of various side products in addition to the desired product. The more specific an enzyme is, the more efficiently the desired chemical reaction will proceed.

Stability
Like all proteins, enzymes can degrade and become non-functional over time or under challenging environmental conditions, such as high heat or pressure. Hyper-stable enzymes can be developed that maintain high activity over long periods of time and in adverse conditions, thus reducing costs associated with adding fresh enzymes.

High-throughput methods
Techniques that allow for parallelized workflows on hundreds, thousands, or even tens of thousands of samples simultaneously. Huge advances in the area of high-throughput methods, tools, and equipment allow researchers to conduct many orders of magnitude more experiments in the same amount of time as was possible just a few years ago and often in a highly automated, reproducible way. This accelerates the pace of research while also reducing costs and increasing the quality of data gathered.

Gene editing
Making a small change to a DNA sequence that already exists within an organism's genome. This process results in the same type of small changes that can be obtained through classical methods, such as breeding, but with a vastly higher level of efficiency and specificity.

Genetic engineering
Introducing a new sequence of DNA into a cell and integrating it into the host cell's own genome. Because all biological systems "read" and "write" using the same genetic code, any gene can be read and understood by its new host. This process results in the same types of genetic changes that can occur naturally through a process called horizontal gene transfer, which is common among free-living microbes and even between microbes and organisms like plants and animals.

constraints of that era's research tools meant that the screening's reach was limited. A systematic effort conducted with today's tools—and bolstered by computational insights based on the wealth of genomic data now available for tens of thousands of microbial species—could yield entirely new candidates for microbial protein production.

The catalog of host strains used as microbial factories for producing high-value targets is also overdue for an overhaul. For decades, the fermentation sector has relied predominantly on a small number of well-established staple species. While there is room to further design these species for higher yields, more robust cultivation, faster growth, and other ideal production traits, the sector has been limited to these species because of their longstanding use and familiarity, as well as regulatory barriers to commercializing new host species.

The urgency of the moment calls for bold research to explore novel hosts that could significantly outperform the incumbents. We also need visionary regulatory leadership to streamline commercial adoption of new candidates. Fermentation must not be stymied by historical allegiance to legacy host strains or outdated regulatory procedures. The alternative protein industry cannot afford it.

Source: Atlast Food Co.

In addition, comprehensive efforts should be undertaken to assimilate systems biology insights regarding metabolic pathways across species to aid in identification and design of novel hosts with ideal attributes. These attributes may include prolonged generational stability to support long-term continuous culture, metabolic pathways that use a wide range of feedstocks, a desirable flavor profile, and low levels of nucleic acid (otherwise levels must be reduced through downstream processing).

Box 4: From the tank to the field: Plants as an expression platform

While most recombinant protein production uses precision fermentation with microbial hosts, crop plants also serve as hosts for production of high-value target molecules. Once engineered, plants can be grown and harvested inexpensively and at large scale through traditional agricultural systems, which may require less infrastructure and therefore less capital expense than most fermentation systems. Upon harvest, downstream purification proceeds much as it would if the host were microbial, although introduction of high-value ingredients into edible plants opens the door to less intensive downstream purification if the crop itself can be used as an ingredient with built-in enhanced functionality. Target molecules for expression in plants might include heme proteins or growth factors for cultivated meat production, such as those pursued by **Core Biogenesis** and **ORF Genetics**. **Mozza** is a pioneer in the category, equipping soybeans to produce milk proteins at agricultural scale. This expression platform will continue to shift both cost and production paradigms and unlock further innovation in recombinant proteins.

Feedstock optimization

Much of the resiliency and adaptability of fermentation derives from its innate malleability with regard to raw material inputs, such as feedstocks. At the same time, feedstocks are the major cost driver for most fermentation processes. Thus, a great deal of optimization is possible in engineering industrial-scale production schemes to use side streams from other industries. This presents potential gains for both economic viability and sustainability.

An increasing number of companies and researchers are capitalizing on precisely this opportunity: the potential to convert waste products or agro-industrial byproducts into high-quality protein biomass. **Nature's Fynd** produces protein from extremophile fungi isolated from a thermal spring in Yellowstone National Park that exhibit wide metabolic flexibility and therefore suitability to diverse feedstocks. 3F Bio and **Mycorena** in Sweden also position themselves as leaders in sustainable feedstock use. Other startups, including Air Protein, leverage gaseous feedstocks, deriving energy from chemical reactions involving hydrogen, methane, or carbon dioxide gas.

Systems biology
An interdisciplinary field that incorporates biological insights and computational and mathematical modeling to develop predictive models of processes occurring within cells.

Generational stability
The phenomenon of predictable, consistent cell performance and behavior across many generations. Any cell culture system will experience slight drift over time as the cells adapt to their production environment. This may eventually interfere with the efficiency or reliability of the manufacturing process, necessitating restarting the process with a fresh sample of the microorganism from a validated starter culture. The longer an organism can remain stable in continuous culture, the more productive and efficient the process will be.

Metabolic flexibility
The ability to selectively turn metabolic pathways on and off in response to environmental conditions. Many microorganisms are able to sense what nutrient sources are present and adapt their metabolism accordingly, allowing them to make use of a wide variety of energy sources.

AIR PROTEIN™

Company highlight: Air Protein

Air Protein uses microbial fermentation to produce human-grade protein directly from CO2 for applications in alternative protein products. Founded in 2019, Air Protein spun out of **Kiverdi**, which applies the same technology for other applications, such as aquaculture feed and biopolymer production. Air Protein is based on a concept first **explored by NASA** in the 1960s as a way to feed astronauts. Air Protein's "closed loop carbon cycle" technology and "probiotic production process" enable the company to create a protein flour that is about **80% protein**—roughly double the content of soy protein flour—with carbon as the primary input. Developing protein production processes that serve as carbon sinks rather than greenhouse gas emitters offers substantial environmental benefits. Watch Air Protein CEO Lisa Dyson's TED talk **here**.

Feedstock optimization should be considered in the context of global shifts in demand across many biological raw materials. The rise in demand for fermentation feedstocks is driven by a wholesale shift toward a bioeconomy model of production leveraging microbial platforms for manufacturing not just food and pharma products but green chemical products, biopolymers, and fuels that have historically been dominated by petrochemical-based production.

Feedstocks should also be examined across all alternative protein production platforms, including plant-based and cultivated. All these production modalities require slightly different feedstocks as primary inputs, and strategic forecasting of raw material demands across all sectors informs better decision-making regarding processing, sourcing, and formulation. Figure 9 illustrates the value of this holistic approach in ensuring that all side streams are accounted for and balanced to maximize profitability, efficiency, and sustainability.

Biomass can be derived from crops grown for purpose or from side streams of bioindustrial or agricultural harvesting and processing.

High-molecular-weight proteins

High utility for **plant-based meat**, egg, and dairy products

Amino acids, small peptides

High utility for **cultivated meat** production; may need to supplement with fermented amino acids

Simple sugars, fiber, and starches

High utility for **microbial fermentation** (production of enzymes, ingredients, protein, etc.) and scaffolding polymers

FIGURE 9. Feedstock sourcing offers opportunities to efficiently leverage side streams across multiple alternative production modalities.

The industry's ability to nimbly tap into diverse, unconventional feedstocks will also be bolstered by the adoption of globally recognized standards and the development of novel characterization technologies. These will give purchasers confidence in the quality and performance of the feedstock material they buy and equip them with the predictive capacity to adapt their process as needed to suit a given lot, even if it is from a source or of a composition they have not routinely used in the past.

Bioprocess design

For decades, microbial fermentation has operated at massive scales, with individual cultivation tanks as large as hundreds of thousands of liters. However, there is still room for innovation in bioprocess design to meet the unique needs of the alternative protein industry.

The vast majority of fermentation facilities currently operational for industrial biotechnology and bioethanol production use submerged fermentation, meaning that the microbial cells are suspended in a liquid nutrient medium. However, some of the structured and intact uses of whole-cell biomass (e.g., whole meat cuts) rely on solid-state fermentation. In this production paradigm, the microbes are inoculated onto a moistened solid feedstock that may be enclosed or grown in open air. These systems may offer cost savings and lower barriers to entry because they do not require the same capital-intensive stainless-steel bioreactors needed for submerged fermentation. Solid-state fermentation platforms also open the door to scale-out approaches rather than scale-up approaches—increasing capacity through parallel small-scale units rather than larger-volume single units, which mitigates the technical risks and capital costs associated with scaling.

Even within submerged fermentation bioprocesses, the scale, cost sensitivity, and sustainability considerations associated with alternative protein applications may warrant approaches distinct from classical stirred-tank bioreactors. Several fermentation companies have successfully commercialized using novel bioprocess and bioreactor designs, but relatively little attention has been paid to further optimization or iteration of these designs simply because few companies have used them to date. Quorn pioneered their commercial launch with a bioreactor design called air-lift fermentation, which requires substantially less energy than conventional bioreactors while accommodating large volumes. This bioreactor design is also well suited for filamentous fungi, which increase the viscosity of the solution more than non-filamentous fungi or bacteria. Animal feed companies using gaseous feedstocks—such as **Unibio** and **Calysta**, who work with methanotrophic bacteria—often apply a similar concept, whereby feedstock gases and other gases circulate the cells and media in an enclosed loop, eliminating the need for an impeller.

Downstream purification and post-harvest processing also fall within this bioprocess design, and these requirements will vary widely according to form and function of the ingredient being manufactured. Current enzyme production provides process and cost benchmarks for future recombinant proteins and other high-value ingredients that require high purity. The purification steps usually account for a substantial fraction of the cost. But for many of the flavoring ingredients or functional proteins used in alternative protein products, high purity may not be necessary. Crushing the host cells without further purification or simply drying the intact cells may be sufficient, depending on several factors: the expression level of the target, the ingredient's use in subsequent manufacturing processes, and the host cell's ability to contribute favorably to the end product's flavor. If whole cells (intact or crushed) are used, many microbial species will require a processing step to reduce the concentration of nucleic acid in the final product.

Air-lift fermentation
A method of submerged fermentation whereby air bubbles are used to mix the cells and ensure uniform access to dissolved gases and nutrients throughout the process. Other methods of mixing include stirring with stainless steel impellers, but this can introduce shear forces that can damage cells, and it also requires energy to operate.

Methanotrophic
Describes organisms that are able to use methane, or natural gas, as their primary nutrient source.

Nucleic acid
The umbrella term for DNA and RNA, the molecules within cells that compose a cell's genome and its transcription into messages that can be decoded as proteins. Fast-growing cells, such as microbial cells, often have higher RNA content than slower-growing cells.

Section 6: Science and Technology Opportunities

Research into retrofitting existing manufacturing facilities and equipment to suit the needs of alternative protein applications is another key opportunity area. Most existing fermentation infrastructure was built for anaerobic fermentation for bioethanol production. As the world moves increasingly toward renewable energy and electrification, these facilities may be decommissioned in the coming decades. However, whether—or under which circumstances—converting them into fermentation facilities for alternative protein applications would be technically feasible or fiscally merited is unclear.

Anaerobic
Occurring in the absence of oxygen. Without proper mixing and aeration, a fermentation culture will eventually become anaerobic. Not all types of microbes tolerate anaerobic growth.

White Dog Labs recently purchased an ethanol plant with **plans to convert it** for aquaculture-feed protein production, which they can do because their microorganism tolerates anaerobic growth. This example illustrates the importance of coordinated R&D efforts across all the key technology development areas to capitalize on insights at the interfaces of these disciplines. Most microorganisms currently used for fermentation for food ingredients require aerobic growth, but if engineering analyses indicate that conversion from bioethanol facilities to anaerobic food production facilities is feasible, then anaerobic growth should be a key screening condition for the comprehensive strain assessment project mentioned earlier in "Strain development."

End product formulation and manufacturing

Fermentation companies that make B2C products have the same opportunities for innovation in formulation and manufacturing as plant-based meat companies. In some cases, additional post-harvest processing steps may be required to endow the microbial biomass with the desired structure and texture. For example, Quorn applies a freezing step to consolidate the delicate mycelial fibers into more durable, aligned bundles that more closely resemble the fibers in animal muscle tissue. Surely there is ample room to develop novel, relatively low-tech and low-cost structuring solutions that can further improve texture without the capital costs associated with the high-moisture extrusion used to produce many current plant-based proteins.

Individual companies will iteratively improve on their products, achieving sensory profiles that more closely mimic those of their animal-derived counterparts by incorporating flavorings, fats, binders, functional enzymes, and nutritional fortification. In turn, many of these ingredients may themselves be produced by B2B providers of fermentation-derived ingredients. Thus, many opportunities for innovation are identical to those of plant-based products (see our **state of the industry report for plant-based meat, eggs, and dairy**).

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Prospects for scaling and cost reduction

Traditional and biomass fermentation processes offer well-established examples of scalability and cost reduction suitable for alternative protein applications. Further innovation to reduce costs is certainly possible for these platforms and will be important for widespread deployment in low- and middle-income countries, but precedent for economic viability and true industrial scale already exists. However, precision fermentation will require additional scaling and cost reduction to manifest its true potential in the alternative protein industry. Some applications of precision fermentation in this industry are already profitable, but others still pose cost challenges.

In fall 2019, economic think tank RethinkX released a **report** on a potential disruption and collapse of the industrial livestock sector. This prediction depends heavily on assumptions regarding diminishing costs and increasing quality of precision fermentation. A key insight underpinning this analysis is that the animal agriculture industry, beef and dairy in particular, is vulnerable to the feed-forward effects of a cascade of disruptions of individual ingredients. While a compelling, marbled cultivated steak is years away, fermentation-enabled versions of less sophisticated products, such as collagen proteins and dairy proteins, may more straightforwardly achieve or exceed the performance and quality of the animal-derived versions. The key, then, is to achieve the scale and technology to undercut the animal-derived versions on cost. The disruption of these animal products, despite being lower-value streams, by fermentation-enabled alternatives represents lost revenue for conventional meat producers. This loss forces conventional meat producers to shift costs to other product streams, a dilemma called the "**carcass balancing problem**." Eventually, by removing revenue from the various animal carcass fractions, the unit economics of animal agriculture will fail to support the industry.

But which price points are achievable for products of precision fermentation, and how quickly? The answer depends on multiple factors, but there is reason to believe that fermentation can achieve price parity with most products through a combination of approaches:

1. **Increasing scale.** Economies of scale dictate that costs decrease as scale increases up to an asymptote where the marginal production cost is equal to the cost of the inputs. Within fermentation processes, returns to scale are especially impressive, as production volumes sometimes span several orders of magnitude. The per-kilogram cost for commercial purified proteins varies by at least **nine orders of magnitude**, from around \$10/kg for many common enzymes to nearly \$10B/kg for specialized proteins, such as those used in therapeutics. Costs may vary by seven orders of magnitude even for proteins involving the same host species.

2. **Improving volumetric productivity.** Volumetric productivity is the amount of desired product that can be produced in a given volume in a given period. For whole-cell biomass, this number simply reflects the growth rate and maximum cell density. For an ingredient produced through precision fermentation, this number also incorporates the titer, which is the expression level of the desired molecule within the host cell.

3. **Prolonging continuous bioprocessing.** Because of the power of exponential growth within cell culture platforms, fermentation processes operate most efficiently and productively at their peak volume and density. The longer a process runs continuously at its peak in steady-state growth, the more efficient the overall run will be because the cells are continuously harvested from their maximum productivity.

4. **Decreasing inclusion levels in the final product.** Alternative protein products benefit from highly functional fermentation-derived ingredients, even at low inclusion levels. For example, the Impossible Burger contains less than 2% heme by weight. While heme may be expensive per kilogram, very little is needed to impart the unique flavor and color of the burger. Similarly, animal-free milk contains only about 3.5% protein by weight (most of the weight is water). An even smaller percentage of recombinant casein or whey protein, supplemented with plant-derived proteins, imparts a sufficiently creamy mouthfeel. Developing ingredients that impart the desired functionality at lower volumes will enable companies to create end products at higher volumes and lower prices.

5. **Relaxing purification stringency.** Many applications of functional proteins in food may not require the same level of purity as active proteins, such as enzymes. As long as the host strain is food-safe and does not negatively impact flavor or texture of the final product, less extensive purification may suffice. Purification composes a substantial fraction of the overall production cost for many recombinant proteins, so relaxing purification requirements will significantly reduce cost.

Section 6: Science and Technology Opportunities

Dozens of enzymes used in food production are manufactured from microbial hosts at large scale. These enzymes serve as benchmarks for achievable prices for alternative proteins from fermentation. Prices for food enzymes typically range from **$1/kg to $100/kg** for relatively pure proteins that are typically used at only a fraction of a percentage by weight of the final product. For comparison, whey protein isolate, which is widely regarded as an inexpensive, high-purity (>90%) protein byproduct of cheesemaking, **typically** costs around $6–$11/kg. Thus, fermentation-derived ingredients are likely to achieve prices that render them economically viable and even competitive with animal-derived proteins for use in many end-product applications.

Substantial scale already exists for microbial fermentation, although how much of this fermentation capacity is suitable for alternative proteins is unclear. A **Deloitte analysis** estimates that the 2020 global fermentation industry will consume about 280 million metric tons of carbohydrate equivalent, of which about 94% will be used for alcohol production (mostly for bioethanol). The remainder will be used for amino acids, organic acids, vitamins, biopolymers, and other chemicals. Notably, of the non-alcohol fraction of fermentation use, most goes toward amino acids primarily used in animal feed. Thus, assuming a major global shift toward alternative proteins in the coming decades, this capacity can be redirected to amino acid production for cultivated-meat cell culture media and repurposed for other fermentation-derived ingredients for alternative protein products. Regardless of the suitability of existing infrastructure, engineering and construction of fermentation facilities is a well-established industry with highly experienced partners in equipment, instrumentation, and operations.

Carbohydrate equivalent
This unit is used to standardize comparisons of feedstock usage across fermentation platforms that use different types of feedstocks (for example, beet sugar and molasses) with different weights and nutrient densities.

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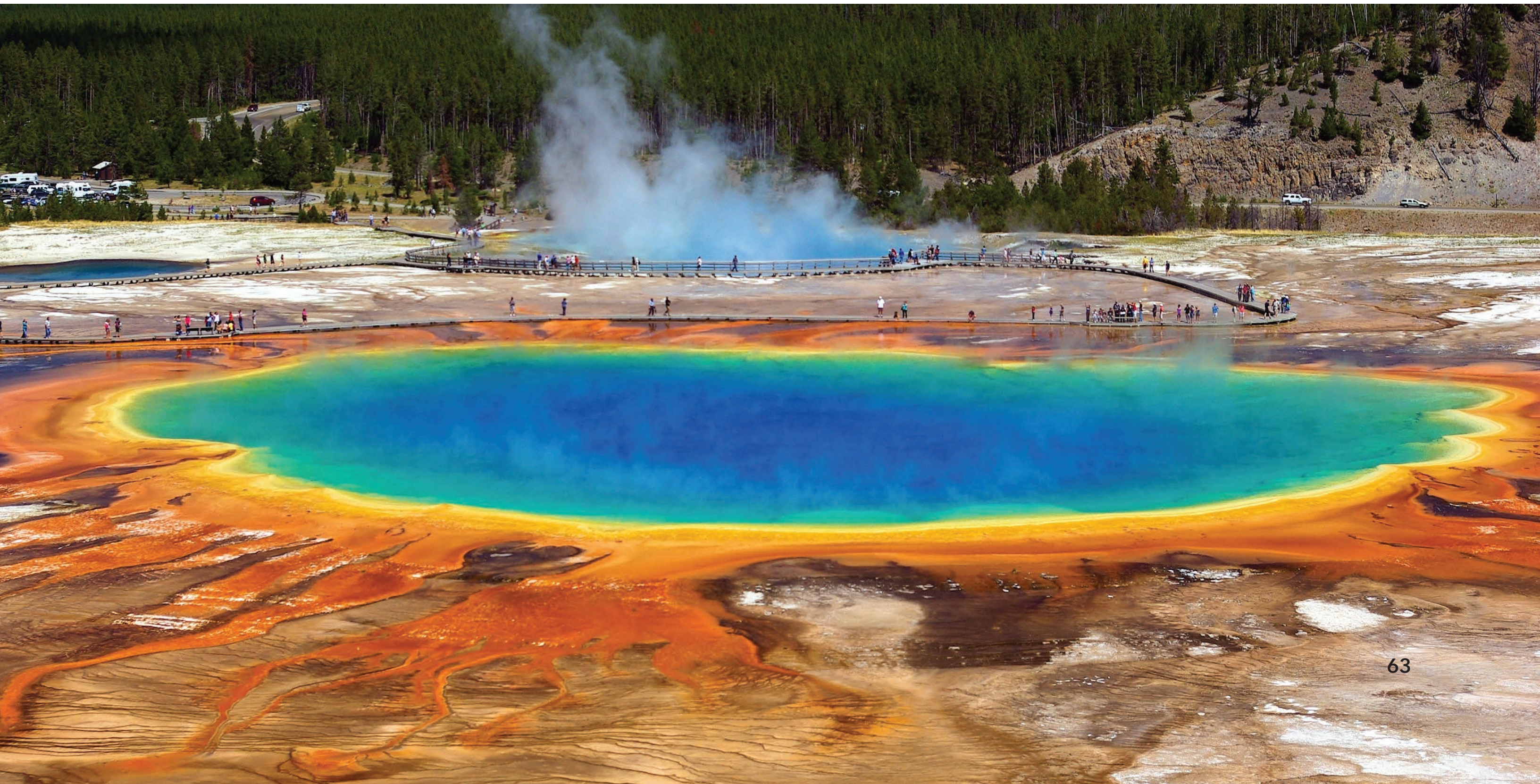
Global outlook and implications

Historically, the United States and Europe have been major innovation hubs for industrial biotechnology and fermentation, particularly from a technology development standpoint. Lately, Asia and Latin America have increasingly positioned themselves as leaders in manufacturing capacity and fermentation infrastructure. With the advancement of new research tools that decrease the cost of R&D, innovation is likely to come increasingly from regions that have not traditionally led biotechnology developments. These regions will be able to couple upstream strain and feedstock improvements with the operational expertise required for swift integration into large-scale manufacturing environments, potentially accelerating the iterative innovation cycle and the path toward cost reduction.

The hot springs in Yellowstone where Nature's Fynd discovered their fermentation engine. Source: Mike Goad from Pixabay. **CEO: "Microbes are pretty damn efficient. They make great protein, and they do it really fast."**



Section 7: Regulatory and Consumer Considerations

Regulatory considerations and success stories

Both microbial fermentation as a processing method and ingredients derived from microbial cultures have a long history of use in the food industry. Given this history, well-established regulatory systems to ensure the safety of innovations within this platform are already in place in most jurisdictions. However, each regulatory agency and framework will present its own nuances and idiosyncrasies. For example, Impossible Foods had to obtain **color additive** approval for their leghemoglobin protein to sell in retail stores but not to sell in restaurants. This is because the FDA took the position that in a raw product sold to consumers, the protein partly serves to impart the characteristic pink of uncooked meat.

Regulations governing the use of genome editing and engineering will also vary by jurisdiction, sometimes restricting certain ingredients outright. However, ingredients that serve as processing aids (e.g., enzymes such as chymosin) are likely to have more leeway in all regions, as many countries exempt processing aids from genetic engineering restrictions. The history of approvals in this area sets precedent and provides clear guidelines for gathering the supporting evidence needed for future ingredients. Additionally, established trade associations have a history of submitting **joint safety dossiers** on behalf of multiple manufacturers. These mechanisms and relationships will ease the regulatory burden of introducing new solutions in this sector.

Multiple companies have already received "no questions letters" from the FDA for purified fermentation-derived ingredients, meaning the FDA does not object to the companies' view that their ingredients are "**generally recognized as safe**" (GRAS). Impossible Foods obtained this **standing** for their leghemoglobin protein as a flavoring ingredient in July 2018 (while the petition for this protein as a color additive required an **additional year**). In April 2020 Perfect Day announced their **GRAS status** for beta-lactoglobulin, the major protein in whey. In part, these approvals were relatively swift because both companies had chosen to use established, food-safe microbial strains as their production hosts. Obtaining regulatory approval for entirely novel strains may be somewhat more laborious. Companies such as Prime Roots and MycoTechnology have positioned their go-to-market strategy around fungal species that have a long history of safe use in food (koji and shiitake, respectively), while other companies, such as Nature's Fynd, are commercializing entirely novel species with no history of consumption. Established analytical methods can test for novel or undesirable components in new strains for both initial safety validation and routine quality control in manufacturing.

Section 7: Regulatory and Consumer Considerations

Labeling and nomenclature

The fermentation sector has not yet aligned on a single term for the process or ingredients derived from it. The various production platforms and use cases of this production modality may be too diverse for a single term. Quorn coined the term "**mycoprotein**" to describe their fungal-derived protein ingredient, but "nutritional fungi protein" or another term may work equally well or better for this type of biomass. Note that as a **settlement** term of a **class action suit**, the company has since modified their packaging in the United States. The allergen warning now reads: "Mycoprotein is a mold (member of the fungi family). There have been rare cases of allergic reactions to products that contain mycoprotein" (even though fungal food allergies are about a thousandfold less common than soy allergies). Perfect Day uses the term "**microflora**" for the microbial hosts and "flora-derived protein" for their animal-free dairy proteins in marketing materials. However, the ingredients disclosure on **Smitten ice cream labels** uses "non-animal whey protein isolate," and the package includes a dairy allergy warning.[2] **MycoTechnology** and other companies that use mycelium from species such as shiitake, whose fruiting bodies are consumed as mushrooms, may be able to use "mushroom protein," "mushroom extract," or similar terms.

Companies could reduce risk of consumer confusion and subsequent regulatory pushback or private litigation by pursuing additional consumer research. As with cultivated meat, developing a clear narrative and using appealing yet informative terms are important when introducing consumers to novel product categories. While the concept of fermentation is widely familiar within food, the ingredients and products pioneered within alternative proteins are often distinct from those most familiar to consumers (e.g., cultured products, such as cheese and yogurt, or alcoholic products, such as beer and wine). Most consumers are unaware of fermentation's role in many familiar foods, ranging from apple juice to bread, as a source of flavorings, enzymes, and vitamins. But all these familiar foods use fermentation systems that are akin to those used in the alternative protein industry. Thus, the potential is high not just for confusion but for familiarity and shared understanding.

2. Note that, unlike probiotic products that also use the term "flora," Perfect Day's products do not contain live cultures.

Fortunately, fermented and cultured foods have recently achieved something of a health halo and a premium status within "foodie" circles, due in part to recent research on the importance of the microbiome to human health and well-being. These positive associations may engender consumer curiosity and receptivity, but use of understandable, accurate terms is still important in describing fermentation's role in alternative protein products. Leaders in this field should invest in collaborative research to determine the terms and narratives that most resonate with consumers while avoiding misunderstandings.

Source: Atlast Food Co.

Section 8: Conclusion

Without alternative proteins, we will be unable to sustainably feed a global population of nearly **10 billion** by 2050. This is because our current system of intensive animal agriculture is inherently inefficient. According to the World Resources Institute, one calorie of chicken meat takes **nine calories of soy, wheat, and corn**; other species of farm animal are even less efficient at converting crop energy into meat energy. This inefficiency has many consequences. For example, according to the Food and Agriculture Organization of the United Nations, industrial animal agriculture **contributes more to climate change than the direct emissions from the entire transportation sector combined**. Livestock is a primary cause of **zoonotic disease** and the **number one consumer** of medically important antibiotics, driving the rise of antibiotic resistance.

Fermentation—use of fungi, microalgae, mycelium, bacteria, and other microbes as bioproduction platforms—has a long history in food production. It is now applied to the alternative protein industry under three primary approaches: traditional, biomass, and precision fermentation. Respectively, these approaches use fermentation as a modularity for improving plant proteins, as a source of high-quality protein-rich biomass, and as a platform for producing high-value specialty ingredients or processing aids. Alongside plant-based proteins and cultivated meat, fermentation has firmly established itself as a pillar of the alternative protein industry. Fermentation provides a vast landscape of innovation potential from both a technical perspective and a product development standpoint.

Fermentation is not just valuable in its own right, offering competitive prices, unparalleled functionality and scalability, and validated mechanisms for establishing and ensuring safety; it stands to revolutionize the entire alternative protein industry, with spillover applications in both plant-based products and cultivated meat. Fermentation can enable a new generation of proteins, fats, and other functional ingredients that combine with plant-based and cultivated components to create biomimicking whole-cut meats, egg replacements, animal-free dairy proteins, seafood products, and more.

These products can exceed the sensory, nutritional, environmental, social, business, and functional paradigms of proteins in the status quo.

Section 8: Conclusion

From a sensory perspective, fermentation can endow end products with taste, mouthfeel, aroma, juiciness, and structure that might otherwise be difficult to deliver. This technology has already helped create a new wave of alternative protein products, such as Perfect Day's ice cream, Meati's steak, and Atlast's bacon. However, very few fermentation companies exist, and even fewer have launched commercial products. The potential to develop fermentation-enabled versions of the thousands of animal products used around the world remains largely untapped.

From a nutritional perspective, fermentation helps deliver high quality at a scale that may alleviate the protein deficit that afflicts much of the world. As well as providing a standalone source of protein, traditional and biomass fermentation increase the digestibility and protein content of plant-based ingredients. Precision fermentation creates essential dietary molecules without raising entire animals to synthesize trace nutrients.

The business case for fermentation is compelling. Fermentation presents a clear opportunity to help transform the multitrillion-dollar animal agriculture market by delivering familiar products more reliably, at a lower production cost, and with enhanced functionality. Animal agriculture margins are thin and at risk. In 2020, the value of large U.S. meat companies fell 25% as Goldman Sachs listed livestock next to oil as one of the **riskiest commodity investments**. Investors would be well served to move their money to alternative protein companies in the fermentation sector, which have collectively raised $837 million in venture capital since 2013.

One of the most exciting business opportunities for entrepreneurs, corporations, and investors is the growing landscape of B2B companies innovating in target molecule selection; feedstock diversification; bioprocess design and construction; or ingredients that enable the broader alternative protein industry, such as ingredients for cost-effective cell culture media for cultivated meat.

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Finally, fermentation may allow us to surpass existing functional paradigms for meat, eggs, and dairy in terms of cook times, handling safety, shelf stability, dry or frozen ingredient storage capability, consumer satiation, ingredient versatility, and more. Currently, most global meat, eggs, and dairy come from a few animal species. However, literally one trillion microbial species remain to be explored for their independent use or for modulating the thousands of edible plant species—an astronomical number of fermentation and plant-protein permutations is possible.

The alternative protein industry has barely scratched the surface of the potential for fermentation-based approaches, and both consumers and existing players within the sector are eager for the innovative products and solutions that fermentation can provide. GFI looks forward to supporting the innovators in this sector as they drive the transformation of our food system into one that is more healthy, sustainable, and just.

Source: Atlast Food Co.

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Source: Meati.

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