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Culturing Health: Next-Gen Fermented Foods for a Thriving Microbiome

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Abstract
Fermented foods have long been celebrated for their sensory diversity and health-promoting potential. Recent advances in microbiome science and food biotechnology are unlocking new possibilities for designing next-generation fermented products that go beyond tradition to target specific health outcomes. This session explores cutting-edge strategies in microbial strain selection, precision fermentation, and functional ingredient fortification to create products that modulate gut microbiota, enhance metabolic health, and support immune function. Topics will include probiotic–prebiotic synergies, fermentation-driven bioactive synthesis, and novel substrates from plant-based and sustainable sources. By bridging traditional fermentation wisdom with omics-based microbial insights and bioprocess engineering, these innovations promise to transform the role of fermented foods from everyday nourishment to precision nutrition tools for a thriving microbiome.

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1. Introduction

Fermentation has remained a cornerstone of human culture for millennia, serving not only as a traditional method of food preservation but also as a means of developing distinctive Flavors while contributing to health benefits. Beyond its cultural significance, fermented foods have long been associated with beneficial effects on digestive health and overall gut microbes. In recent years, modern food science and biotechnology are transforming the landscape of fermentation through precision-driven approaches by understanding of the complex interplay between diet, gut microbes, and human health. These insights have catalysed the convergence of traditional wisdom and cutting-edge science promises to redefine fermented foods as strategic tools for precision nutrition, moving beyond general wellness toward personalized health interventions. Advances in microbial strain engineering, omics technologies, and bioprocess optimization are driving the development of next-generation fermented foods designed to achieve targeted physiological outcomes. Unlike traditional methods that relied on spontaneous microbial activity, these strategies leverage controlled fermentation to enhance probiotic viability, boost bioactive synthesis, and incorporate functional ingredients such as prebiotics. Such advancements hold potential to address critical health concerns, including metabolic disorders, immune modulation, and gut health restoration, thereby positioning fermented foods as tools for improving health benefits.

A wide variety of traditional fermented foods are consumed globally, most of which are produced through natural fermentation and continue to be prepared using age-old methods that remain largely unchanged even today. Some common traditional fermented foods are shown in Fig. 1. Technological advancements and sustainable, plant-based alternatives have emerged as key drivers in the evolution of fermentation science. The integration of novel substrates derived from legumes, cereals, and agro-industrial by-products supports both environmental and nutritional goals, reducing reliance on animal-based inputs while minimizing food system waste. Furthermore, the application of omics-based analytics and artificial intelligence in fermentation

process optimization represents a convergence of traditional knowledge with advanced scientific technologies. Collectively, these innovations promise to redefine fermented foods, transforming them from conventional dietary components into precision nutrition tools capable of promoting a resilient and thriving microbiome.

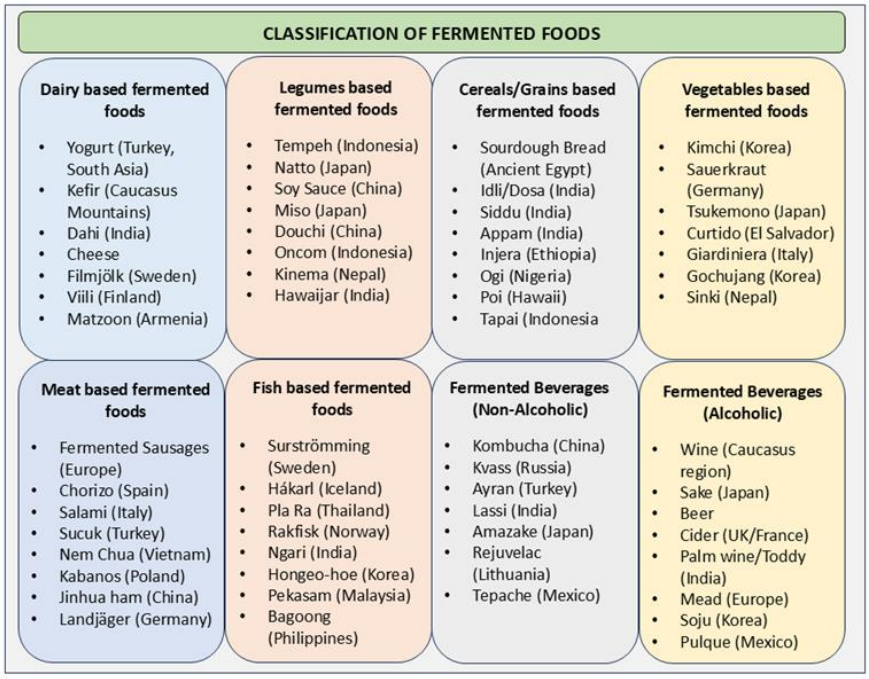

Fig 1: Classification of fermented foods

The gut–food axis encompasses a multifaceted interaction between dietary inputs and the gut microbiome, in which food-derived substrates regulate microbial activity and metabolic outputs that collectively shape host physiology and long-term health. Fermented foods and beverages have been an integral part of human diets for thousands of years, primarily employed for food preservation and safety, owing to the production of inhibitory metabolites such as organic acids. The human gut is a dynamic ecosystem where fermented foods shape microbial composition, influencing nutrient assimilation, energy harvest and the production of bioactive metabolites that influence systemic health. Fermented foods represent a critical node in this connection by delivering both live microorganisms and pre-digested bioactive compounds that can enhance gut physiology more effectively than non-fermented foods. Over the years, numerous scientists have investigated fermentation to unlock its full potential and enhance fermentation strategies. Key milestones in this field include Louis Pasteur's work from 1856 to 1878, which demonstrated the critical role of yeasts in alcoholic fermentation and showed that lactic acid fermentation is carried out by specific microorganisms, proving that microbes, not chemical processes, are responsible for sugar conversion. In 1876, German microbiologist Herman Ahlburg identified the Koji mold (*Aspergillus oryzae*), laying the foundation for controlled Koji fermentation used in producing sake, miso and soy sauce. Eduard Buchner's 1897 discovery that fermentation could occur via enzymes outside living cells further established the enzymatic basis of fermentation, paving the way for modern industrial and biotechnological applications.

Table 1: Overview of commonly fermented foods, highlighting their primary microorganisms, key biochemical and nutritional transformations, and associated health benefits

Fermented Food	Key Microbes	Biochemical / Nutritional Changes	Major Health Outcomes	References (2022–2025)
Yogurt	*Lactobacillus delbrueckii, Streptococcus thermophilus*	Lactose → lactic acid, release of bioactive peptides, increased folate, B vitamins, and free amino acids (proline, glycine), enhanced protein digestibility.	Improved lactose tolerance, antihypertensive effects, significantly reduced prevalence of nutrient deficiencies for riboflavin, vitamin B-12 and minerals like calcium, magnesium, and zinc, improve probiotic gut microbiota modulation and gut immunity	Adolfsson *et al*. (2024)
Kefir	*Lactobacillus kefiranofaciens, Lactococcus lactis, yeasts (Saccharomyces, Kluyveromyces)*	Mixed lactic acid & alcoholic fermentation; Lactose → lactic acid by lactic acid bacteria, yeasts ferment sugars to ethanol and CO_2, production of kefiran, biopeptides, vitamins (B_{12}, Riboflavin/B_2), and essential amino acids (valine, isoleucine, methionine, serine, threonine, phenylalanine, tryptophan, alanine, lysine)	Reduced lactose intolerance; improved gut health via probiotic-rich functional food, immune modulation, antioxidant, antimicrobial, and anti-inflammatory activities, antihypertensive effects; anti-diabetic and hypocholesterolemic properties	Saleem *et al*. (2023)
Dahi (Indian	*Lactococcus lactis,*	Lactose → lactic acid; enrichment of	Reduced lactose intolerance; better	

curd)	*Lactobacillus plantarum, Leuconostoc mesenteroides (varies regionally)*	probiotics; enhanced bioavailability of calcium, iron, and B-vitamins (B_2, B_5, B_{12}), production of free fatty acids, conjugated linoleic acid (CLA), and essential amino acids (methionine, lysine, tryptophan, leucine)	digestion, reduced gastrointestinal discomfort, probiotic health benefits, beneficial for diabetics, antimicrobial activity, increased antioxidant activity, immune enhancement, antihypertensive, cholesterol-lowering, and antiatherogenic effects	Mudgal & Prajapati., (2017)
Cheese	*Lactococcus, Lactobacillus, molds (Penicillium)*	Lactose → lactic acid; proteolysis → peptides; lipolysis → free fatty acids; B-vitamin enrichment rich source of high-quality protein (mainly casein), lipids, minerals (calcium, phosphorus, and magnesium), and vitamins (vitamin A, K_2, B_2, B_{12}, and folate), and probiotics and bioactive molecules (bioactive peptides, lactoferrin, short-chain fatty acids, and milk fat globule membrane)	Antihypertensive peptides, probiotic benefits, supports muscle growth and development, blood pressure regulation, dietary calcium for bone development, nutrient-dense	Zhang *et al.* (2023)
Sauerkraut	*Leuconostoc mesenteroides, Lactobacillus plantarum, Lactobacillus brevis*	Carbohydrates → lactic acid, formation of bioactive isothiocyanates from glucosinolates and other bioactive peptides, production of vitamins C & K	Gut microbiota modulation, improved digestion, source of probiotic bacteria, antioxidant activity; immune support, protection against oxidative DNA damage	Peñas *et al.*, (2017)
Kimchi (vegetables)	*Leuconostoc mesenteroides, Lactobacillus plantarum, L. mesenteroides, Pediococcus*	Lactic acid fermentation of vegetables with added salt, production of organic acids (mainly lactic acid), increased ascorbic acid (vitamin C) content, hydrolysis of starch and other polysaccharides to smaller molecules, formation of bioactive compounds	Gut microbiota regulation, improved bowel movement, antioxidant, anti-inflammatory, and anti-obesity effects; reduction of adipose tissue weight and adipocyte size; reduction of serum total cholesterol, triglycerides, and LDL cholesterol, regulation of serum lipid profiles, insulin, leptin, and adiponectin levels; immune cell development and inflammatory response control, anticancer potential (≈80% inhibition)	Cheigh *et al.*, 1994; Patra *et al.*, (2016)
Kombucha	*Acetobacter ssp (Acetobacter aceti, Acetobacter xylinum, Gluconobacter spp., Acetobacter pasteurianus) yeasts (Saccharomyces, Brettanomyces)*	Sugars → ethanol and acetic acid; fermentation of sugared tea with SCOBY, polyphenol biotransformation and oxidation of polyphenolic compounds, catechins, and flavonoids; production of organic acids (gluconic and glucuronic acids), bioactive compounds like vitamins (B-complex, C, E, K), and amino acids (theanine, glutamine)	Gut microbiota enrichment; improved digestion and gut health; antioxidant detoxification and liver support, reduction of blood pressure and cholesterol, weight management, kidney and gallbladder health, enhanced immune response, skin benefits (combat acne, reduce wrinkles), improved bowel movement	Bishop *et al.*,2022
Tempeh	*Rhizopus oligosporus, R. oryzae, R. stolonifera, Lactobacillus ssp*	soy proteins → peptides & amino acids, Protein hydrolysis, vitamin K2 enrichment, vitamin B12 synthesis, reduction of antinutrients (phytates, trypsin inhibitors, tannins, oligonucleotides, lectins)	Enhanced protein digestibility, enhanced amino acid availability, improved nutrient absorption and bioavailability, probiotic effect, bone and cardiovascular health, anti-diabetes effects, cognitive function improvement, anti-aging effect, antidepressant effects	Teoh *et al.*,2024
Meso	*Aspergillus oryzae, lactic acid bacteria (Lactobacillus, Ente rococcus, and Pediococcus),* yeast (Zygosaccharomyce s rouxii, Saccharomyces rouxii and Torulopsi)	Soy proteins → peptides and amino acids; reduction of antinutrients (phytates), production of bioactive compounds (SCFAs, vitamin B_{12}), high protein content (32–42%, mainly glycinin and β-conglycinin), soybeans naturally contain isoflavones, while miso provides their biologically active aglycone forms (genistein, daidzein), enriched with polyamine spermidine and its precursor putrescine.	Antioxidant activity, gut microbiota regulation, flavour enhancement, improved digestion, enhance immunity and, metabolic health benefits (cholesterol and glucose regulation)	Allwood *et al.*, (2021)
Natto	*Bacillus subtilis var. natto*	Soy proteins → nattokinase, peptides and aminoacids Soy isoflavone glycosides to aglycones, Vitamin K2 (menaquinone-7) synthesis	Cardiovascular health (blood clot prevention, control of blood cholesterol levels, prevention of arterial sclerosis, heart disease, and hypertension), enhanced digestion, probiotic benefits, promote bone development and growth	Afzaal *et al.*, 2022
Sourdough (wheat/rye bread)	*lactic acid bacteria (Lactobacillus sanfranciscensis, Lacticaseibacillus casei,*	Starch → lactic & acetic acids; protein hydrolysis, B-vitamin & B12 enrichment, improved mineral bioavailability via phytic acid hydrolysis (Zn^{2+}, Mg^{2+}, Ca^{2+}, Mn^{2+}, Cu^{2+}, Fe^{2+})	Improved digestibility, lower glycemic index, gut microbiota modulation, enhanced protein digestibility and fiber utilization.	Alkay *et al.*, 2024

	Levilactobacillus brevis),Yeasts (Saccharomyces cerevisiae, Saccharomyces chevalieri, Candida milleri)			
Idli / Dosa batter (fermented rice-lentil)	*Lactiplantibacillus plantarum, Saccharomyces cerevisiae, Leuconostoc mesenteroides*	Starch breakdown → lactic acid; reduction of antinutritional phytates (increase in the (%) of - zinc 50–71%, iron 127–277%), enrichment in organic acids, partial protein hydrolysis, increased B-vitamins (folate, pyridoxine, niacin, riboflavin, thiamine, B12	Improved mineral bioavailability (iron, zinc), better glycemic control, improved digestibility, enhanced nutrient absorption, mild probiotic benefits, production of exopolysaccharides (EPS) and bacteriocins	Ramalingam *et al.*, 2019; Hemalatha, 2007
Appam (rice + coconut, toddy starter)	*Saccharomyces cerevisiae, Candida tropicalis, LAB, Bacillus cereus*	Starch → lactic acid & ethanol, mild alcohol + organic acids, flavor and aroma compounds, leavening and soft texture, reduction of phytates, enrichment in B-vitamins, fermentation of carbohydrate such as maltose, trehalose, xylose, cellobiose, and galactose	Easy digestibility; mild probiotic benefits, energy-dense, supports quick energy release, enriched in B-vitamins, improves mineral bioavailability (iron, zinc)	Pal *et al.*, 2005
Gundruk (fermented leafy vegetables)	*Lactobacillus plantarum, Leuconostoc mesenteroides, Lactobacillus fermentum, Lactobacillus casei*	Lactic acid fermentation; sugars in leafy vegetables into lactic acid, high vitamin C and bioactive compounds, improved mineral bioavailability, enhanced flavor	Low-calorie content for weight management, high fiber for digestive health, gut health, antioxidant activity, anti-inflammatory.	Ghatani *et al.*, 2024
Fermented soy paste (Doenjang, Doubanjiang)	*Aspergillus oryzae, Bacillus subtilis, LAB*	Soybean protein → various amino acids and peptides, starch → organic acids, B-vitamin & K	Antioxidant, gut health, flavour enhancement, anti-obesity effects, anti-hyperlipidemic and glucose-metabolism benefits	Woo *et al.*, 2023
Pickles (vegetable & fruits -mango, carrot, cucumber, pineapple, cherry)	*Lactobacillus plantarum, Leuconostoc spp., Pediococcus spp., Bacillus spp., Saccharomyces cerevisiae, Stenotrophomonas spp.*	Carbs → lactic acid, vitamin enrichment	Gut microbiota support, antioxidant activity, constipation inhibition, antimicrobial effects, anti-inflammatory effects	Tan *et al.*, 2023
Fermented meat (salami, sausages)	*Lactobacillus sakei, Lactobacillus casei, Lactobacillus paracasei, Staphylococcus carnosus, Penicillium nalgiovense (mold).*	Proteolysis → peptides and release of essential amino acids (threonine, valine, leucine, lysine), Lipolysis → free fatty acids with reduced saturated fatty acid (SFA) and cholesterol content, and increased monounsaturated fatty acid (MUFA) content; Bioactive compounds present (taurine, carnosine, histidyl dipeptides, Vitamins B-complex)	Flavor development, mild probiotic benefits, improved digestibility, reduction of biogenic amine formation, antihypertensive effects, antioxidant effects, immunomodulatory effects, enhanced nutrient availability, improved fat metabolism, cholesterol reduction	Bou *et al.*, 2017
Fermented fish (Pla ra, Surströmming)	*Halophilic bacteria (Halanaerobium, Lentibacillus), Lactobacillus plantarum, Pediococcus spp., Tetragenococcus spp., Staphylococcus spp., yeasts (Saccharomyces, Candida)*	Proteolysis → peptides and release amino acids (glutamate, aspartate, glycine, alanine), Lipolysis and oxidation → free fatty acids converted to hydroperoxides with variable changes in lipid profile (increase in SFAs and MUFAs, decrease in PUFAs), Mineral enrichment (calcium, potassium, sodium, and magnesium)	Enhanced digestibility, unique flavor development, probiotic potential, antioxidant activity, antimutagenic effects, antihypertensive activity, anticancer potential (e.g., reported in Utonga-kupsu), probiotics for gut health	Singh *et al.*, 2018; Chan *et al.*, 2023
Wine	*Saccharomyces cerevisiae, Lactobacillus spp.*	Sugars →ethanol, organic acids, polyphenols, malic acid → lactic acid, increase in high-density lipoprotein (HDL) cholesterol, enrichment in polyphenols.	Antioxidant activity, cardiovascular support in moderate consumption, improved gut microbiota modulation, reduction in risk of cardiovascular disease, atherosclerosis, and hypertension, increase in HDL cholesterol aiding cholesterol clearance, modulation of immune function and inflammation, excessive consumption	Guilford & Pezzuto., (2011) Bacillus subtilis

			linked to adverse health problems	
Naturally fermented alcoholic beverages- Beer (wheat or barley), Toddy (palm sap), Sake (rice), and Cider (apples), Mead(honey)	*Saccharomyces cerevisiae (ale), Saccharomyces pastorianus (lager), Saccharomyces chevalieri, Pichia fermentans, Saccharomyces rosei, Saccharomyces fructuum, Lactobacillus spp., Brettanomyces spp., Acetobacter spp., Bacillus spp., Aspergillus oryzae, and Oenococcus oeni. Leuconostoc*	Sugars → ethanol and CO_2, starch (in beer and sake) → sugars via enzymatic saccharification, malic acid → lactic acid (malolactic fermentation), organic acids, polyphenols, B-vitamin enrichment, lipid oxidation producing minor flavor compounds	Safe and nutritious, provide refreshment and energy, enhance digestibility, contain bioactive flavor compounds, exhibit antioxidant activity, offer moderate benefits of alcohol, show mild probiotic effects (notably in sour beers), and may help alleviate insomnia, headaches, body aches, inflammation, diarrhea, urinary issues, and expel intestinal parasites, excessive consumption linked to adverse health problems	Kumari *et al.*, 2016; Lodolo *et al.*, 2008; Aparnna *et al.*, 2024; Mendes-Ferreira *et al.*, 2010; Zhang *et al.*, (2020); Calugar *et al.*, 2021
Non-alcoholic fermented beverages- Kvass (cereal), Boza (cereal), Chicha (corn), Tapai (rice), Amazake (rice), Tepache (pineapple), Rejuvelac (sprouted grains), Mahewu / Mageu (maize/cereal).	*Lactobacillus spp. (L. plantarum, L. rhamnosus, L. pentosus, L. paracasei, L. fermentum, L. brevis, L. sakei), Pediococcus spp., Streptococcus spp., Saccharomyces spp., Rhizopus spp., Acetobacter spp., Aspergillus oryzae.*	Carbohydrate fermentation → lactic acid, trace ethanol, starch → sugars (in Chicha, Tapai, Amazake), organic acids, B-vitamin enrichment (B1, B2, B6), bioactive peptides, dietary fiber, polysaccharides, sterols, amino acids, fatty acids, improved mineral bioavailability (Fe, Ca, Mg, K, Zn, P)	provides micro- and macronutrients, improves nutritional status, supports digestion, modulates gut microbiota, exhibits mild probiotic effects, antioxidant activity, regulates metabolism, reduces flatulence and hyperacidity, lowers blood pressure, mitigates hypertension, decreases cholesterol, supports immune function, enhances skin health, reduces risk of obesity and cancer, and offers benefits in diabetes.	Ignat *et al.*, 2020

Fermented foods are distinctive in that they generally comprise both viable microorganisms (or their cellular components) and a range of fermentation-derived metabolites, including short-chain fatty acids (SCFAs), polyphenol derivatives, exopolysaccharides and microbial peptides, which collectively exert functional effects on the gut. Natural fermentation is typically a spontaneous process, initiated by indigenous microorganisms originating from the raw substrate, the surrounding environment, utensils or through the addition of pre-established starter cultures. From a biochemical point of view, fermentation is a metabolic process carried out by microorganisms that primarily convert carbohydrate molecules in the substrate to generate energy (ATP) for survival and produce metabolic end-products (ethanol, acetic acid, lactic acid and CO_2) to regenerate NAD^+ for subsequent glycolytic cycles. Most of the microorganisms involved in fermentation mainly belong to lactic acid bacteria (LAB), yeasts and sometimes filamentous fungi. They metabolize carbohydrates, proteins and lipids into a spectrum of biomolecules with unique texture, flavour, enhancing nutrient bioavailability and functional properties to the product. Microbial activity enhances the nutritional quality of fermented products by degrading antinutritional factors such as phytic acid, synthesizing vitamins, releasing bioactive peptides along with their precursors, while also producing organic acids, exopolysaccharides, essential amino acids and short-chain fatty acids, all of which contribute to product preservation as well as improve host health by regulating metabolic balance and supporting gut homeostasis. The overview of commonly fermented foods is shown in Table 2. Fermented foods are generally easier to digest because microbial enzymes partially hydrolyse complex macromolecules during fermentation, leading to enhanced protein digestibility, breakdown of starch and other polysaccharides into smaller molecules, improved amino acid availability and reduced levels of antinutritional factors that otherwise hinder nutrient absorption in the gut. For example, in dairy-based fermented foods such as yogurt, dahi and kefir, lactic acid bacteria break down lactose and milk proteins, enhancing digestibility and improving nutrient bioavailability for easier absorption. Lactose intolerance arises from insufficient intestinal β-galactosidase (lactase activity), leading to maldigestion and gastrointestinal problems. Fermentation of milk to yogurt reduces lactose concentration by 20–30% through microbial hydrolysis, while partial conversion of glucose to lactic acid further decreases the lactose load. Importantly, *Lactobacillus bulgaricus* and *Streptococcus thermophilus* express functional lactase, which remains active in the gut and facilitates in situ lactose hydrolysis. These microbial contributions explain the improved tolerance of yogurt compared to milk among lactose-intolerant individuals (Goodenough and Kleyn, 1976; Adolfsson *et al.*, 2004). Yogurt contains a higher protein concentration than raw milk because of the addition of nonfat dry milk solids and the concentration steps involved in processing. The fermentation process improves protein digestibility through bacterial proteolysis, which liberates free amino acids such as proline and glycine. Furthermore, casein coagulation, along with the retention of whey proteins, enhances the biological quality of yogurt proteins and supports more efficient intestinal nitrogen utilization compared with milk (Gaudichon *et al.*,

1995). Most dairy products constitute rich sources of B vitamins, folate and essential minerals, including calcium, potassium, phosphorus and zinc. Fermentation modulates B-vitamin content, as specific lactic acid bacteria strains can synthesize folate and vitamin B12, thereby increasing their levels (Buttriss, 1997). Several studies suggest that calcium derived from fermented dairy products, especially from yogurt, contributes more effectively to bone mineralization than calcium from non-fermented sources (Kaup *et al*., 1987).

Soy fermented products, widely consumed across Asian countries including China (douchi, sufu, doubanjiang, jiang, furu), India (kinema, hawaijar, tungrymbai, bekang), Japan (natto, miso, tofu, soy sauce/shoyu), Korea (doenjang, cheonggukjang, gochujang, kanjang, meju), Indonesia (tempeh, tauco, oncom), the Philippines (tao-si), Vietnam (tuong, banh dau) and Thailand and Laos (thua-nao) are valued not only for their nutritional content but also for their probiotic potential and beneficial effects on gut health. Fermentation of soybean-based products improves nutritional quality by increasing levels of essential amino acids, synthesizing vitamins, reducing anti-nutritional factors and producing enzymes that hydrolyze proteins, cellulose and carbohydrates, thereby enhancing digestibility and detoxifying harmful compounds. In tempeh and miso, *Rhizopus* and *Aspergillus* species facilitate the degradation of phytic acid, thereby enhancing the bioavailability of essential minerals, including iron, potassium and zinc. Moreover, *Rhizopus* spp. in tempeh contribute to the production of vitamin B12, polyphenols and antioxidant compounds, whereas *Bacillus* spp. in natto are primarily responsible for increasing vitamin K_2 levels (Kamao *et al*., 2007; Mo *et al*., 2023). Fermented soy foods are rich in antioxidant compounds such as polyphenols, flavonoids, saponins and sterols, which protect against oxidative stress and enhance overall health, highlighting the multifaceted benefits of soybean fermentation. Prebiotic fibres in fermented foods help digestion and promote bowel movements in the small intestine, improving overall food digestion. Fermented foods, especially soy and rice, contain prebiotic oligosaccharides and soluble sugars, including raffinose family oligosaccharides (sucrose, raffinose and stachyose), which are metabolized by microbial enzymes, as mammals lack the $\alpha 1 \rightarrow 6$ galactosidase enzyme required for their digestion (Kumar *et al*., 2010; LeBlanc *et al*., 2008).

In cereal-based fermentations, LAB break down complex starches and proteins into simpler compounds, such as smaller peptides, amino acids and organic acids, thereby improving digestibility and overall nutritional quality. Sourdough fermentation improves the nutritional and functional quality of grain-based foods by enhancing LAB-driven proteolysis, stimulating cereal proteases through organic acid production, thereby promoting protein hydrolysis that releases bioactive peptides, amino acids and metabolites, while also modifying gluten structure and lowering glycemic responses. Notably, *Lactobacillus sanfranciscensis* possesses glutathione reductase, which plays a crucial role in maintaining redox balance, stabilizing proteins and supporting the sustainability of the yeast population (Xu *et al*., 2018). Sourdough fermentation lowers the estimated glycemic index (eGI) of products by reducing postprandial glycemic and insulin responses through acidification, which delays carbohydrate digestion and glucose absorption, and inhibition of saccharification reactions that generate hyperglycemic substances (Özer *et al*., 2023). Synergistic LAB–yeast fermentation alters starch granule morphology through acidification and protease activation, degrading intact granules and inducing cracks while preserving crystalline structures that resist full hydrolysis. Together, these effects highlight the role of sourdough as a natural bio-processing system that enhances protein bioavailability while moderating starch digestibility and glycemic impact in cereal products (Wang and Wang, 2024).

Vegetable fermentations (e.g., sauerkraut, kimchi) rely on natural microbial consortia that degrade plant fibers, produce short-chain fatty acids and release phenolic compounds with antioxidant activity. Similarly, the fermentation of fish and meat using traditional methods enhances flavor and texture, reduces biogenic amine accumulation, improves fat metabolism and increases digestibility, thereby improving nutrient absorption. Overall, plant- and animal-based fermented foods undergo distinct biochemical modifications driven by microbial activity, which not only extend shelf life but also enhance the nutritional and functional quality of the final product. During fermentation, complex macronutrients and anti-nutritional factors are broken down into bioactive compounds, including simple sugars, peptides, amino acids, vitamins, short-chain fatty acids (SCFAs), phenolics, essential minerals and precursors of various biomolecules, which exert beneficial effects and are more readily absorbed in the gastrointestinal tract. These metabolites also exhibit strong probiotic effects by promoting gut microflora, while organic acids produced during fermentation regulate intestinal pH, inhibit pathogens, support beneficial microbes such as *Lactobacillus* and *Bifidobacterium* and strengthen intestinal barrier integrity to enhance immune function. Moreover, fermentation enhances unique flavor, aroma and texture, increasing consumer acceptance. By integrating food structure, microbial activity and host physiology, fermentation serves as a key driver of the gut–food axis, offering opportunities to develop next-generation functional foods that improve gut health and the nutritional quality of foods.

2. Designer Microbes: Targeting Health with Precision

The advances in synthetic and molecular biology techniques have enabled the development of designer microbes, which are genetically engineered microorganisms tailored to perform targeted therapeutic functions and support precision nutrition. Unlike conventional probiotics, a new link forged by integrating synthetic biology with fermentation science is giving rise to engineered strains that extend the traditional roles of fermentation beyond preservation and flavor, positioning them within the realm of precision health. Conventional probiotics and other fermented products generally offer broad, non-specific benefits, such as enhancing nutrient absorption, improving the digestibility of food components, supporting gut microbiota balance and contributing to the production of bioactive molecules in the gut. Genetically modified microbial strains employed in fermentation can be engineered to provide tailored nutritional and therapeutic benefits. These fermentation-derived strains have potential applications in targeted drug delivery, cancer-specific probiotics, urogenital and skin health, immune modulation and infection prevention. By enabling such precise interventions, they transform fermentation from a conventional source of nutrition into a platform for advanced therapeutic modulation, thereby redefining the dynamic

interplay between diet, the microbiome and health outcomes (Patra, 2016). The application of omics tools (genomics, transcriptomics and metabolomics) enables researchers to employ precision fermentation approaches to identify generally recognized as safe (GRAS) microorganisms with beneficial genes or reprogrammed metabolic pathways, supporting functions such as vitamin biosynthesis, antimicrobial peptide production, hydrolysis of anti-nutritional factors and the synthesis of metabolites like short-chain fatty acids, thereby moving beyond reliance on traditional spontaneous or starter culture fermentations.

The synthetic biology strategy in this arena involves strain engineering, where designer microbes are modified to enhance their beneficial outputs for the development of probiotics with therapeutic applications. Techniques employed in GRAS microbes include targeted genome editing (CRISPR-Cas, TALENs, ZFNs), metabolic pathway engineering, synthetic circuit design, plasmid-based systems and classical mutagenesis or adaptive/directed evolution to optimize functional traits and metabolite production. The development of CRISPR-Cas systems has revolutionized probiotic engineering by enabling precise genetic modifications, in which targeted insertions or deletions induce double-strand DNA breaks that are subsequently repaired via non-homologous end joining (NHEJ) or homology-directed repair (HDR) pathways (Liu, 2023; Li *et al*., 2022).

CRISPR-Cas systems are pervasive across prokaryotes, detected in approximately 85% of archaea and 42% of bacterial species (Plagens *et al*., 2022). Within the *Lactobacillus* genus, complete CRISPR-Cas systems are present in over 40% of species, with certain taxa exhibiting particularly high prevalence, such as *Lactobacillus crispatus* (96%) and *Lactobacillus delbrueckii* (93%), while others, including *Lactobacillus ruminis*, show more moderate occurrence (~41%). Notably, around one-third (32%) of *Lactobacillus salivarius* (*Ligilactobacillus salivarius*) harbor type III CRISPR-Cas systems (Roberts and Barrangou, 2020; Crawley *et al*., 2018). In the genus *Bifidobacterium*, CRISPR-Cas systems are observed in 57% of strains, spanning multiple subtypes, including I-E, I-C, I-G, II-A and II-C (Pan *et al*., 2020). CRISPR–Cas9 systems delivered through plasmids, carrying the Cas9 nuclease, a single-guide RNA and optionally a donor template, enable precise genome modifications in probiotics, including the insertion of antigenic sequences in *Lactobacillus acidophilus* for oral vaccine development, disruption of the antibiotic resistance gene *tetW* in *Bifidobacterium animalis* subsp. *lactis* and targeted self-elimination of spoilage or pathogenic bacteria such as *Lactobacillus buchneri* (Hidalgo-Cantabrana *et al*., 2017). Using native Type I and II CRISPR-Cas systems, *Lactobacillus* strains can be precisely engineered into designer probiotics, enhancing their therapeutic potential for immune modulation and targeted biotherapeutic delivery, thereby providing tailored health benefits (Goh and Barrangou, 2019). Fang *et al*. (2024) engineered the probiotic *Escherichia coli* Nissle 1917 using a type I-E CRISPR-Cas system to block the transfer of multiple antibiotic resistance genes (ARGs), thereby reducing ARG spread in the gut microbiome and improving the safety and therapeutic efficacy of the probiotic.

Synthetic gene circuits act as “smart” delivery systems, enabling engineered probiotics to release therapeutics in a controlled manner in response to specific environmental cues or physiological stressors, such as changes in pH, temperature, glucose or other biomolecules within the body (Zhao *et al*., 2023). Engineered probiotic *Lactobacillus reuteri* biosensors using *Staphylococcus aureus* agr quorum sensing detect AIP-I in real time, enabling rapid monitoring of infections. These sensors have potential applications in hospital pathogen detection and high-throughput drug screening (Lubkowicz *et al*., 2018). A research study by Mao *et al*. (2018) showed that engineered *Lactococcus lactis* probiotics reduce intestinal *Vibrio cholerae* burden in mice by producing lactic acid, thereby enhancing colonization resistance. They also enable point-of-need detection by sensing chimeric CqsS-NisK quorum signals, enabling early-stage infection identification through analysis of fecal samples and offering significant potential for disease prevention and surveillance in at-risk populations. Heme-sensitive probiotics, including *Escherichia coli* Nissle 1917, were engineered to detect intestinal bleeding in pigs using fluorescence-based readouts, providing accurate diagnosis of gastrointestinal haemorrhage. Integrated into ingestible micro-bio-electronic devices (IMBEDs) with miniaturized luminescence electronics, these probiotics enable in situ biomolecular monitoring and offer a modular, extensible platform for gastrointestinal disease detection and management (Mimee *et al*., 2018).

Plasmid-based systems are a widely used method for developing genetically modified microbes. Through this method, designer microbes with therapeutic potential are developed by engineering probiotics with synthetic pathways for targeted treatments such as antimicrobial peptide production and anti-inflammatory compounds, while boosting hydrolytic capacity to degrade proteins, lipids and carbohydrates into simpler units, thereby improving biomolecule synthesis and mineral bioavailability. Plasmid-based systems offer controlled gene expression and precision therapies; however, plasmid use also raises concerns of horizontal gene transfer, which researchers address through containment strategies like kill-switch mechanisms, underscoring both the promise and biosafety challenges of plasmid-engineered probiotics (Kazi *et al*., 2022; Carnes, 2005).

Engineered probiotics are being developed as a cutting-edge approach in oncology, designed to release chemotherapeutic agents at the tumor site while minimizing harm to surrounding healthy tissues during conventional chemotherapy (Chua *et al*., 2017). Engineered *Bifidobacterium longum* expressing pBBAD-Tum (BL-Tum) selectively targets hypoxic colon cancer cells and delivers Tumstatin to inhibit vascular endothelial cell proliferation and induce apoptosis. This targeted strategy effectively reduces tumor growth and microvessel density, demonstrating its potential as a precise antitumor gene delivery system (Wei *et al*., 2016). Engineered probiotic *Saccharomyces boulardii* expressing fibronectin-targeting ligands and anti-TNF nanobodies selectively localizes to inflamed colonic mucosa and reduces inflammation-associated tumorigenesis in colitis-associated colorectal cancer. This approach decreases tumor burden and colon inflammation, demonstrating its potential as a targeted therapeutic strategy (Culpepper *et al*., 2025). A study by Chung *et al*. (2021) demonstrated that engineered *Pediococcus pentosaceus* expressing the therapeutic protein P8 selectively targets colorectal tumors, reduces tumor growth and polyp formation and restores gut microbial

balance, highlighting its potential as a targeted probiotic therapy for colorectal cancer. Engineered probiotics are likely to play a key role in cancer therapy, as advanced strains with precise, controlled drug-delivery systems broaden their applications across different cancer treatments.

Engineered designer microbes are emerging as versatile tools for advancing health across multiple domains, with primary applications in therapeutic drug delivery, immune modulation and infection prevention. Their scope further extends to the treatment of autoimmune diseases, allergic reactions, metabolic and endocrine disorders, while also offering innovative interventions for mental health and neurological disorders. In the gastrointestinal tract, engineered probiotics can treat inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) by delivering anti-inflammatory agents or neurotransmitter precursors directly at inflammation sites, improving therapeutic outcomes, supporting gut microbiota balance and minimizing systemic side effects (Patra, 2024). Engineered *Lactococcus lactis* was developed to treat inflammatory bowel diseases by delivering IL-10 protein through a stress-inducible controlled expression system and IL-10 cDNA via a host-targeted cassette. These dual systems ensured localized IL-10 production at mucosal sites, reducing colitis severity in TNBS-induced mice and improving weight recovery, colon integrity and immune balance (Del Carmen *et al*., 2014).

Probiotic designer microbes targeting mental health and neurological disorders may enhance cognitive function and emotional well-being by modulating gut microbiota, reducing neuroinflammation and delivering neurotransmitters such as serotonin and GABA. Engineered probiotics provide targeted approaches for managing metabolic disorders by regulating blood glucose, enhancing lipid metabolism, controlling appetite, improving insulin sensitivity and supporting weight management. For example, engineered *Lactobacillus plantarum* NC8 was developed to express angiotensin-converting enzyme inhibitory peptides (ACEIPs) by fusing sequences from tuna frame protein (TFP) and yellow fin sole frame protein (YFP) using an arginine linker in the pSIP409 vector. Oral administration of this recombinant strain in spontaneously hypertensive rats significantly lowered systolic blood pressure, endothelin and angiotensin II levels, while increasing nitric oxide levels, demonstrating its potential as a safe and effective probiotic therapy for hypertension (Yang *et al*., 2015).

Engineered probiotics face numerous challenges and limitations in therapeutic applications, including biological, safety and clinical translation issues. The use of GMOs as therapeutic probiotics raises biosafety and regulatory concerns, necessitating containment strategies such as "suicide genes" or "kill-switches" and extensive clinical trials to ensure safety, efficacy and public trust. Biological challenges include degradation in the stomach, competition with native microbiota and the need to survive acidic gastrointestinal environments. Strategies such as pH-sensitive polymers and encapsulation can enhance survival, but personalized immune responses and difficulties in large-scale production continue to complicate their development (MacCorkle *et al*., 1998; Mandell *et al*., 2015; Gheorghita *et al*., 2021; Garcia-Brand *et al*., 2022; Zheng *et al*., 2025). These challenges can be addressed through advancements in precision engineering, AI-guided design, gene-editing tools and encapsulation technologies, enabling personalized probiotics tailored to individual microbiomes with enhanced stability and targeted functionality for metabolic and other health conditions. Overcoming these barriers through interdisciplinary and sustainable solutions positions engineered probiotics as a cornerstone for advancing safe and effective therapeutic applications in the future.

3. Probiotic–Prebiotic Partnerships for Synergistic Benefits

The The integration of probiotics and prebiotics, commonly referred to as synbiotics, represents a promising frontier in the development of next-generation fermented foods, offering a strategic approach to enhance their functional potency and promote human health. Probiotics, defined as live microorganisms that offer health benefits when consumed in adequate amounts, play a crucial role in modulating the gut microbiota, inhibiting pathogenic organisms and supporting immune function. The concept of probiotics holds great importance in medicine today, but its history dates back to around 13,000 BC, when people unknowingly consumed fermented foods. Fermented foods serve as natural sources of probiotics generated through microbial activity, which not only improve nutrient bioavailability but also enhance the synthesis of bioactive compounds and contribute to maintaining a balanced gut environment. The term probiotic is derived from the Greek words *pro* and *bios*, meaning "for life" or "promoting life." The concept of probiotics was first proposed in 1907 by Nobel Prize winner Elie Metchnikoff, who suggested that the longevity of Bulgarian peasants was linked to their consumption of fermented milk products (Petrova *et al*., 2021). Later, in 1965, Lilly and Stillwell used the term "probiotic" to describe substances secreted by one organism that stimulate the growth of another (Lilly and Stillwell, 1965).

The gut microbiota is a complex community of commensal microorganisms that maintain a symbiotic relationship with the host, contributing to nutrient metabolism, immune modulation and protection against pathogens, thereby supporting overall host health. The concept of probiotics, prebiotics and synbiotics in the diet helps improve the gut microbiota and harness its metabolic and therapeutic potential. Fermented foods are rich in probiotics, including lactic acid bacteria (*Lactobacillus rhamnosus*, *Lactobacillus reuteri*, *Lactobacillus casei*, *Lactococcus lactis*, *Lactobacillus plantarum*), *Bifidobacterium* species, *Lactococcus*, *Streptococcus*, *Enterococcus* and yeasts like *Saccharomyces boulardii* and *Saccharomyces cerevisiae*. Probiotic strains must be non-pathogenic and possess GRAS status as regulated by the FDA and guidelines by WHO. Moreover, they should remain genetically stable, with the capacity to survive in the gastrointestinal tract by tolerating acidic and bile conditions and rapidly produce beneficial metabolites (Pandey *et al*., 2015; Markowiak and Śliżewska, 2017). Dairy-fermented products, especially yogurt, are among the best sources of probiotics. They contain lactic acid–fermenting bacteria, beneficial microorganisms that improve gut microbiota and overall gastrointestinal health. The clinical benefits of probiotics have been widely documented and include: (i) alleviation of gastrointestinal disorders such as diarrhoea and inflammatory bowel disease; (ii) inhibition of pathogenic microbes in the gut (suppression of *Helicobacter pylori*); (iii) improves the nutritional value of food through the release of free amino acids, synthesis of vitamins and production of other bioactive compounds that

promote health; (iv) enhanced digestibility of proteins, carbohydrates and lipids through partial hydrolysis into peptides, amino acids, short-chain fatty acids and other small metabolites; (v) regulation of serum cholesterol levels and other metabolic parameters; (vi) prevention of allergic reactions by strengthening the intestinal barrier and modulating immune responses through induction of regulatory cytokines (e.g., IL-10, TGF-β) and inhibition of IgE-mediated pathways; (vii) anti-cancer effects by modulating gut microbiota and host immunity; (viii) reduction of lactose intolerance symptoms in milk product consumption; and (ix) stimulation of gut-associated immune responses via the interaction of lactic acid bacteria with the mucosal epithelial lining of the gastrointestinal tract (Parvez *et al*., 2006; Farrell *et al*., 2025; Adolfsson *et al*., 2004; Markowiak and Śliżewska, 2017).

Table 3: Overview of biotic components and their fermented food sources.

Term	Definition	Key Feature / Activity	Example Microbes / Compounds	Fermented Food Example	Reference
Probiotics	Live microorganisms that provide health benefits when consumed in adequate amounts	Must be viable; act directly in the gut, improves gut microbiota, inhibiting pathogenic organisms, and supporting immune function, releveling lactose tolerance, anti-inflammatory effect	*Lactobacillus*, *Bifidobacterium*	Yogurt, kefir, kimchi,	Gupta and Garg (2009)
Prebiotics	Non-digestible food components (primary dietary fibers) that selectively stimulate growth/activity of beneficial microbes in the gut	Serve as food/energy for gut microbes, improves bowel movement, enhance production of short-chain fatty acids (SCFAs), improve gut barrier function and overall gut health, hypercholesterolemic effect, enhanced mineral bioavailability	Inulin, Fructo-oligosaccharides (FOS), *Galacto-Oligosaccharides* (GOS), Trans-galacto-oligosaccharides (TOS)	Fermented oatmeal, fermented soy, sourdough, pickled garlic/onion	Davani-Davari *et al*. (2019)
Synbiotics	Combination of probiotics and prebiotics with synergistic effects	Enhance survival and metabolic activity of beneficial microbes in intestinal microbiota, provide greater health benefits than probiotic or prebiotic alone, inhibition of potential pathogens presents in the gut, hepatic detoxication, prevention of osteoporosis, improves immunity, enhance SCFA production	*Lactobacillus brevis* PML1+ inulin, *Weissella cibaria* FB069 +xylooligosaccharides	Fortified yogurt + insulin, foetified soymilk + xylooligosaccharides , Kombucha-Based Drink Enriched with Inulin and Vitamins	Falah *et al*. (2021); Isakov *et al*. (2023); Markowiak and Śliżewska (2017); Pandey *et al*. (2015); Lee *et al*. (2020)
Postbiotics	Postbiotics are defined as preparations of inanimate microorganisms and/or their components that confer health benefits to the host. Since postbiotics do not contain live microorganisms, they are generally more stable and present fewer safety risks compared to probiotics.	Bioactive metabolites or non-living microbial components and fragments, enhance immunomodulatory effects in the gut, anti-atherosclerotic activity, antitumor activity, accelerate wound healing	CFAs, aromatic amino acids, phenolic-derived metabolites, bacteriocins, peptides, enzymes, vitamins, folate, bacterial lysates, exopolysaccharides	Fermented dairy supernatants	Żółkiewicz *et al*. (2020)
Parabiotics	Inactivated (non-viable) microbial cells or fragments that confer health benefits	Dead cells still beneficial, reduce risks associated with consumption of live microorganisms, exert immunomodulatory effects, antimicrobial activity, antioxidant activity, help lower cholesterol, triglycerides, and blood sugar levels, anti-obesogenic, and anti-hypertensive effect	Heat-killed Lactobacillus	Heat-treated fermented milk	Lee *et al*. (2023)
Metabiotics	Bioactive compounds or signalling molecules produced by microbes, including structural elements of probiotic microorganisms and their metabolites, with defined chemical structures that can modulate host-specific physiological functions,	Can act therapeutically without live microbes, y, beneficial effects on human health and immune system, which is important for the prevention and control of bacterial and viral infections, safety, and long shelf-life	SCFAs, polyamines, tryptophan metabolites, polysaccharides, peptidoglycans, teichoic acids, lipo- and glycoproteins, vitamins, antioxidants, amino acids	Fermented soy or dairy extracts (bifidobacteria and lactobacilli), Kefir, metabiotric drinks (‘Zakofalk, Hylak Forte)	Fan *et al*. (2022)

	regulatory or metabolic processes, and behaviour, in connection with the activity of the host's native microbiota				
Psychobiotics	Probiotic microbes can synthesize or modulate neuroactive biomolecules, such as GABA and serotonin, thereby promoting mental health benefits through the gut–brain axis.	Health benefits for patients with psychiatric illness, antidepressant activity, educe hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis, anti-inflammatory actions, Cognitive enhancement, Improved metabolic or hormonal balance	*Lactobacillus rhamnosus*, *Bifidobacterium longum*, *Bifidobacterium infantis*, *Lactobacillus casei*	yogurt, probiotic-containing milk, Kombucha, kefir	Bravo *et al*. (2011); Benton *et al*. (2007); Dinan *et al*. (2013); Göbel and Doğan (2023)
Probioceuticals / Probiotic nutraceuticals	Probioceuticals are probiotic-derived biologically active compounds with targeted health benefits that positively influence human health.	Designed for therapeutic purposes, targeting antitumor effects and anti-inflammatory activities, enhance metabolic activities	Probiotic capsules for cholesterol management or immune support; exopolysaccharides (EPS) – lactic acid bacteria (LAB); reuterin – *Lactobacillus reuteri*	Fortified probiotic drinks, curd, cheese	Kumar *et al*. (2020); Nataraj *et al*. (2020)

Prebiotics are primarily non-digestible dietary fibres that selectively promote the growth and activity of beneficial gut microorganisms, thereby supporting host health. Unlike probiotics, prebiotics do not contain live microbes; common examples include inulin, fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS) and trans-galacto-oligosaccharides (TOS), which are often incorporated into fermented foods such as yogurt. These compounds confer multiple health benefits, including improved bowel regularity, reduced incidence and duration of diarrhea, attenuation of gut inflammation and enhanced mineral absorption. Moreover, prebiotics contribute to the regulation of intestinal barrier integrity, modulation of host metabolism and immune function, lowering of certain cardiovascular risk factors, promotion of satiety and weight management and potential reduction in colon cancer risk (Davani-Davari *et al*., 2019; Peña *et al*., 2007; Pokusaeva *et al*., 2011).

Synbiotics refer to the combined administration of probiotics and prebiotics, which synergistically enhance gastrointestinal function by improving the survival and metabolic activity of beneficial intestinal microbes and providing greater health benefits than either probiotics or prebiotics alone. The synergistic action of both prebiotics and probiotics provides a more comprehensive approach to modulating gut microbiota. The combined action of live beneficial microbes along with the substrates that selectively promote their growth enhances colonization, survival and activity within the gastrointestinal tract. Numerous research studies are ongoing in the field of synbiotics, exploring how the combined effects of probiotics and prebiotics can be harnessed for targeted therapeutic applications, particularly in cardiovascular health, prevention of insulin resistance in elderly patients, inflammatory bowel disease, metabolic disorders and antibiotic-associated dysbiosis (Falah *et al*., 2021; Isakov *et al*., 2023; Markowiak and Śliżewska, 2017).

Probiotic, prebiotic and synbiotic formulations are increasingly being incorporated into next-generation functional foods and nutraceuticals to enhance their health-promoting potential. Moreover, the concept of probiotics has evolved beyond general gut health toward targeted therapeutic functions. New categories such as parabiotics, postbiotics, metabiotics (Shenderov, 2013), psychobiotics and probioceuticals (probiotic nutraceuticals) have been developed to deliver the beneficial components of probiotics while reducing risks associated with live microorganism consumption. These formulations provide precise nutrition and targeted therapeutic delivery, exerting immunomodulatory and other health-promoting effects. The various concepts and types are summarized in Table 3. The incorporation of designer microbes via genetic engineering accelerates therapeutic applications by enabling targeted delivery of drugs and bioactive molecules that improve metabolic health, modulate immunity, exert anti-inflammatory effects and address nutrient deficiencies. Psychobiotics, a class of probiotic microbes, can synthesize or modulate neuroactive biomolecules such as GABA and serotonin, thereby promoting mental health benefits through the gut–brain axis. These effects include support for patients with psychiatric disorders, antidepressant activity and enhancement of cognitive function (Bravo *et al*., 2011; Benton *et al*., 2007; Dinan *et al*., 2013; Göbel and Doğan, 2023). Overall, the development of probiotics, prebiotics and synbiotics represents a promising strategy to promote health through targeted therapeutic interventions and disease prevention, offering a modern perspective beyond the traditional concept of gut microbiota modulation.

4. Omics and AI in Fermentation Science

Fermentation practices are rooted in traditional knowledge, but recent advancements in omics technologies and artificial intelligence (AI) have profoundly transformed the landscape of fermentation science. Traditional fermentation processes, once guided largely by empirical knowledge, are now being refined through data-driven and predictive systems-based methodologies. The integration of AI with omics-driven insights provides a deeper understanding of microbial diversity, metabolic pathways and community dynamics, enabling precise control and optimization of fermentation processes. These advanced tools also contribute to a comprehensive understanding of functional food development and the safety assessment of novel foods derived from recombinant microorganisms. Moreover, they

enhance the safety, quality attributes and nutritional value of fermented products, paving the way for more reliable and health-oriented food innovations. Integrated omics approaches, including genomics, transcriptomics, proteomics and metabolomics, offer a holistic understanding of the diversity, functions and dynamic roles of fermenting microorganisms, while AI and machine learning (ML) enable advanced data analysis and predictive modelling of fermentation processes (Singh and Kumar, 2025; Chen *et al*., 2017).

Omics approaches provide a comprehensive framework for understanding the biological mechanisms underlying fermentation by analysing the genetic blueprint of microorganisms, encompassing genomic, transcriptomic, proteomic and metabolomic datasets, and enabling precise strain identification and functional gene characterisation through modern high-throughput methodologies. Different omics technologies are used in fermentation science to understand microbial communities during fermentation. Table 4 shows the different omics technologies applied to study fermentation processes. Genomics, transcriptomics, proteomics and metabolomics provide insights into microbial functions at the molecular level, while community-wide approaches such as metagenomics, metatranscriptomics and metaproteomics reveal the collective dynamics of microbial consortia. Specialised omics such as peptidomics and lipidomics further enrich understanding of nutritional, sensory and health-related attributes.

Table 4: Omics approaches used in fermentation science with examples.

Omics Approach	Use in Fermentation Science	Examples in Fermented Foods	Reference
Genomics	Decodes DNA sequences of microorganisms, revealing the genetic blueprint of fermentative microbes (e.g., identifying species and functional genes).	*Lactobacillus* strains in yogurt, *Saccharomyces cerevisiae* in sake and wine.	Akao *et al*. (2011); Fu *et al*. (2021); Alexandraki *et al*. (2020)
Transcriptomics	Profiles messenger RNA (mRNA) to show which genes are actively expressed during fermentation, shedding light on metabolic responses under certain conditions.	Stress response genes in beer brewing yeasts, lactic acid metabolism in cheese.	Gu and Zhao (2019); Wu *et al*. (2022)
Proteomics	Catalogs the proteins and enzymes produced by microbes, indicating the biochemical activities driving fermentation reactions.	Protease activity in cheese ripening; Flavor formation and enzyme production occur during soy sauce fermentation	Chen *et al*. (2020); Bouroutzika *et al*. (2021); Zhao *et al*. (2018)
Metabolomics	Maps small-molecule metabolites and flavor compounds, offering a direct view of the fermentation's chemical outcomes.	Flavor compounds in kimchi; organic acid profiles in sourdough bread.	Alseekh *et al*. (2021); Lee *et al*. (2024); Sun *et al*. (2025)
Metagenomics	Uses shotgun DNA sequencing to identify the collective microbial population in a ferment, including unculturable species.	Microbiome diversity in kombucha; microbial communities in tempeh.	Coughlan *et al*. (2015); Pangastuti *et al*. (2019); Kaashyap *et al*. (2021)
Metatranscriptomics	Extends transcriptomic analyses to microbial communities, linking community-wide gene expression to functional activity.	Gene expression dynamics in kimchi fermentation; yeast-bacteria interactions in wine,flovour producing microbes in tradition fermented soyabean pate (dajiang)	An *et al*. (2021); Lee *et al*. (2022); Tang and Peng (2024); Liu *et al*. (2020)
Metaproteomics	Profiles community-level protein expression to elucidate interspecies interactions and active metabolic functions during fermentation, thereby linking genetic potential with expressed biochemical activities	Applied in analysing protein expression in kefir grains, mixed-culture fermentations in beer, optimization of maize fermentation through functional protein mapping, metaproteomic characterization of fermented vegetables.	Chen *et al*. (2020); Zhang *et al*. (2024); Bahule *et al*. (2022)
Peptidomics	Studies bioactive peptides, contributing to health-promoting properties (neuroprotection, antihypertensive, antidiabetic, and anti-inflammatory activities) and sensory attributes in fermented foods.	Antihypertensive, antidiabetic, and anti-inflammatory peptides in fermented milk; bioactive peptides in miso, neuroprotective peptides in fermented soybean	Chourasia *et al*. (2023); Zhang *et al*. (2025); Pipaliya *et al*. (2024)
Lipidomics	Profiles fatty acids and lipids, enriching understanding of flavor, texture, and health attributes in fermentation.	Lipid changes in fermented sausages; fatty acid profiles in fermented fish.	Chen *et al*. (2023); Gao *et al*. (2024); Wang *et al*. (2025)

In addition to the major omics presented in Table (2), several emerging approaches are increasingly utilized in fermentation research, including volatilomics, which characterizes volatile compounds contributing to aroma and flavor development; glycomics, which investigates sugars and glycoproteins associated with microbial growth, food quality, and nutrient dynamics; ionomics, which evaluates the mineral and elemental composition influencing microbial metabolism; fluxomics, which traces intracellular metabolic fluxes to enhance fermentation efficiency; and phenomics, which assesses phenotypic variations under different fermentation conditions. (Chang *et al*., 2025; Tang *et al*., 2022; Watanabe *et al*., 2013; Peltier *et al*., 2018). By integrating various omics technologies (multi-omics), researchers can connect genes, their activity, and the metabolites they produce, offering a comprehensive view of fermentation. This approach provides deeper insights into microbial interactions, metabolism, and flavor development (Ferrocino *et al*., 2023). Overall, omics technologies reveal the intricate mechanisms underlying fermented food production, allowing a system-level understanding of microbial metabolism and interactions, and facilitating improved strain selection and process optimization.

The metagenomics studies helped in detecting hundreds of

microbial species and their physiological changes involved with traditional fermentation. For example, 131 bacterial groups were identified fermenting olives, with early salt-loving microbes later replaced by Lactobacillales and others (Medina *et al*.,2016). Multi-omics helps to understand which microbes were involved in flavour. In cheese, specific microbes were associated with the production of aromatic compounds. In Chinese baijiu, certain bacteria produce organic acids which enhance its taste. Omics technologies were also combined with tools like CRISPR to select strains with desired and to improve starter cultures (Pan *et al*., 2020). In the study by Wu *et al*., (2023), a multi-omics strategy integrating transcriptomics, proteomics, and metabolomics was applied to elucidate the molecular basis of soy sauce-like and soybean flavor formation in *Bacillus subtilis* BJ3-2. The combined omics data revealed temperature-dependent modulation of amino acid transport, secondary metabolite biosynthesis, and metabolic pathway regulation associated with distinct flavor profiles. This comprehensive approach provided a deeper mechanistic understanding that can aid in optimizing fermentation conditions for improved flavor development.

In fermentation science, the use of Artificial Intelligence (AI) has increased recently to extract patterns from complex datasets, improve process parameters, and even predict microbial behavior (Kyodo News, 2018). Computer vision and machine learning have been employed in traditional brewing. Recent developments in digital technologies have introduced digital twin systems as effective tools for supervising and optimizing fermentation processes. In kombucha production, Zhao *et al*., (2025) reported the development of a digital twin framework that combines data from interconnected sensors with computational modeling to predict the parameters pH, aeration, bacterial counts, sugar level, microbial activity, and overall process performance. The model integrates multi-scale feature extraction and a genetic algorithm–based control strategy, enabling precise prediction and regulation of fermentation behavior. By linking the virtual fermentor model to real-time data inputs, the system enables continuous monitoring and adaptive control, thereby enhancing consistency and efficiency in the fermentation process. In white wine fermentation, Florea *et al.*, (2022) employed an AI-based system a pre-trained multilayer perceptron neural network optimized with genetic algorithms to predict alcohol and substrate concentrations from variables such as temperature, time, and biomass. The system automated process monitoring, reduced manual measurements, enhanced prediction accuracy, and demonstrated the potential of AI-driven tools to optimize fermentation management in the wine industry. In kimchi fermentation, artificial intelligence optimizes wireless sensor placement for efficient monitoring of temperature and humidity, while Long Short-Term Memory (LSTM) deep learning models analyze the data to predict changes in acidity and ripeness, thereby improving process management, maintaining consistent product quality, and reducing the need for manual supervision (Kim *et al*., 2024). The microbial interactions within a fermentation process can be predicted using AI, and deep learning can help determine which two different microorganisms will grow and interact in co-culture under various conditions. These models can predict strain compatibility and microbial interactions (competitive or symbiotic) even before co-fermenting them (Singh & Kumar., 2025). These are examples of the range of AI applications transforming fermented food production. Moreover, AI technologies are driving real-time decision-making, process optimization, and quality validation in fermentation to achieve efficient and reliable outcomes.

Artificial intelligence has become a pivotal tool in precision fermentation, enabling the accurate prediction and optimization of complex bioprocesses. Machine learning approaches, such as neural networks, support vector machines, and Gaussian process regression, are increasingly applied to model intricate relationships between experimental parameters and fermentation outcomes. By leveraging data-driven surrogate models, AI facilitates rapid experimentation, streamlines scale-up, and reduces reliance on time-consuming physical trials. When integrated with metabolic modeling and high-throughput omics data, these methods allow for precise manipulation of microbial pathways and targeted strain improvements. Collectively, these advancements enhance process control, increase product yield, improve resource efficiency, and contribute to the development of sustainable, robust, and scalable fermentation systems.

The microbial interactions within a fermentation process can be predicted using AI, and deep learning can help determine which two different microorganisms will grow and interact in co-culture under various conditions. These models can predict strain compatibility and microbial interactions (competitive or symbiotic) even before co-fermenting them (Singh & Kumar., 2025). These are examples of the range of AI applications transforming fermented food production. Lastly, AI technologies are driving real-time decision-making, process optimization, and quality validation in fermentation to achieve efficient and reliable outcomes (Vinestock *et al*., 2024). Integrating omics technologies with AI is enabling us to achieve new levels of understanding and control in fermented food science. The integration of omics technologies and artificial intelligence is providing unprecedented insights and control over fermented food systems. While omics identifies microbial composition and functional activity, AI interprets complex datasets to guide process optimization. This integrated approach transforms fermentation from conventional trial-and-error methods to predictive, data-driven strategies, influencing both traditional and modern probiotic foods, and advancing the overall field of fermentation technology.

5. Sustainability of New-Generation Fermented Foods

The sustainability of new-generation fermented foods lies at the convergence of technological innovation, targeted nutritional benefits, and environmental stewardship, reflecting their critical role in shaping a resilient and resource-efficient modern food system. New-generation fermented foods like plant-based ferments, precision fermentation products (such as animal-free dairy proteins), mycoproteins (fungal proteins like Quorn™), kombucha, and cultivated meat, genetically modified microorganisms designed to enhance fermentation efficiency or nutritional quality, and dairy alternatives are solutions in building a sustainable food system. They open new possibilities in reducing environmental impacts to food waste while serving consumer demands for a healthier diet. Traditional livestock farming is one of the major contributors to greenhouse gas emissions (GHG), land use, and water consumption (Knychala *et al*., 2024). Unlike traditional fermentation, these modern foods utilize advanced microbial consortia,

optimized processing, and underutilized plant-based substrates to enhance nutritional value, functional properties, and sensory appeal while minimizing waste and resource consumption. By integrating AI along with biotechnological tools and omics-driven insights (genomics, proteomics, metabolomics), production can be precisely controlled, improving efficiency and reducing energy and raw material use. Furthermore, valorization of agro-industrial by-products and incorporation of eco-friendly practices align these foods with circular economy principles, making them not only health-promoting but also environmentally and economically sustainable. As global demand for functional, eco-conscious foods grows, new-generation fermented products exemplify a pathway toward resilient, sustainable, and future-ready food systems.

The global population is steadily rising, currently estimated at approximately 7.6 billion and projected to reach 8.6 billion by 2030 and 9.8 billion by 2050 (United Nations, 2017). This unprecedented demographic expansion presents a major global challenge, exerting immense pressure on agricultural resources, food supply systems, and the environment. Consequently, the conventional model of food production is becoming increasingly unsustainable, necessitating the adoption of innovative, sustainable strategies to ensure long-term food and nutritional security. Traditional livestock farming is one of the major contributors to greenhouse gas emissions (GHG), land use, and water consumption (Knychala *et al*., 2024). In this context, plant-based fermented foods have emerged as a promising alternative due to their lower environmental footprint, nutritional richness, and functional properties. These foods not only contribute to environmental sustainability but also provide numerous health benefits, being rich in bioactive compounds such as peptides, polyphenols, flavonoids, phytochemicals, and vitamins, as well as beneficial probiotic microorganisms that support gut health and overall well-being. Additionally, fermented foods exhibit a wide range of therapeutic effects including antioxidant, anti-inflammatory, antidiabetic, antihypertensive, and cholesterol-lowering activities that collectively contribute to disease prevention, metabolic regulation, and overall human health (Dhiman *et al*., 2025; Sahoo *et al*., 2023).

New-generation fermented foods are redefining global food systems by integrating environmental efficiency, nutritional enhancement, and circular bioeconomy principles. Eco-friendly fermentation processes, including solid-state systems for lignocellulosic residues, reduce energy and water consumption compared to conventional methods. Fermentation is considerably more efficient than conventional farming, as microorganisms such as fungi, yeasts, and bacteria exhibit rapid growth rates compared to the months or years required for animal rearing (Knychala *et al*., 2024). For example, the production of mycoprotein demands significantly less water and land while yielding high-quality protein more efficiently than livestock-based systems (Souza Filho *et al*., 2019). Mycoprotein, a protein-dense food derived primarily from the biomass of filamentous fungi, such as *Fusarium venenatum*, has emerged as a sustainable alternative to conventional animal-derived meat products. It is recognized as one of the most promising next-generation protein sources owing to its high nutritional value, minimal environmental impact, and potential to reduce global dependence on livestock farming (Wiebe, 2002). Additionally, its production results in substantially lower greenhouse gas emissions compared to traditional meat production. This is particularly relevant as over 30% of anthropogenic greenhouse gas (GHG) emissions originate from agricultural activities, with livestock production alone contributing approximately 14–18% of the total (Steinfeld *et al*., 2006; Smetana *et al*., 2015).

Mycoprotein, produced from fungi, exhibits notably lower environmental impacts than animal-based proteins such as beef, chicken, or pork (Souza Filho *et al*., 2019). Quorn™ mycoprotein mince has been reported to generate approximately thirteen times fewer greenhouse gas emissions than beef (Green Stars Project, 2020). Unlike livestock production, fungal fermentation directly converts raw materials into protein without methane emissions, further enhancing its environmental sustainability (Smetana *et al*., 2015). Industrially, they are cultivated under aerobic conditions in large-scale bioreactors using carbohydrate-rich substrates or agro-industrial residues, followed by fungal biomass harvesting, heat treatment to reduce nucleic acid content, and texturization to mimic the fibrous structure of meat (Finnigan *et al*., 2019; Wiebe, 2002). Moreover, the use of low-cost agro-industrial residues as substrates not only reduces production costs but also promotes waste valorization and supports circular bioeconomy principles (Satari & Karimi., 2018). Nutritionally, mycoprotein provides a complete amino acid profile, is rich in dietary fiber (notably β-glucans and chitin), and contains minimal saturated fat attributes associated with improved lipid metabolism, reduced cholesterol, and better glycaemic regulation in consumers (Souza Filho *et al*., 2019). Thus, mycoprotein production exemplifies how microbial fermentation can simultaneously address environmental sustainability and human nutritional needs, marking a significant advancement toward sustainable protein alternatives in the global food system. Precision fermentation allows microorganisms like yeast to produce specific proteins and many therapeutic compounds. These products only require 90% less land and 96% less water, with GHG emissions reduced by up to 97% (Knychala *et al*., 2024). Cultivated meat could cut carbon emissions by 44–92% compared to beef or pork, while using up to 90% less land (Sinke *et al*., 2023). New-Gen fermented foods have strong potential to reduce environmental impacts.

Fermentation is an old traditional method for preserving foods such as milk, vegetables, and grains, reducing food waste. It can turn surplus food into long-lasting products like yogurt, pickles, or kimchi (Smetana *et al*., 2015). Kombucha can be brewed using leftover fruit peels or spent coffee grounds, transforming waste into beverage (Villarreal-Soto *et al*., 2018). Human health is a part of sustainability; all fermented foods have high nutritional benefits. Fermented plant products break down anti-nutrients, increasing mineral absorption, and produce vitamins and antioxidants (Dhiman *et al*., 2025). Kombucha and kefir contains beneficial microbes that improve digestion and boost immune function. Fermentation can also produce “postbiotics”, bioactive compounds with positive health effects (Fraiz *et al*., 2025). Dairy proteins produced through precision fermentation have same high-quality amino acids as milk without lactose or cholesterol. Fermentation also cuts poor feed conversion rates of animals, while livestocks only convert a fraction of their feed to proteins. The microbes in fermenters convert most of their raw feed into proteins with higher efficiency year around, independent of seasons or weather, ensuring

constant food supply (Sinke *et al*., 2023). New-generation fermented foods present a better alternative for creating a strong and sustainable food system. These foods minimize land and water use, lower greenhouse gas emissions, enhance production efficiency, reduce food waste, and provide nutritionally enriched products. By integrating traditional fermentation knowledge with modern biotechnological innovations, fermentation stands as a key strategy for achieving global food security and sustainability in the future.

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