

Review

The food microbiome: an evolutionary architect, a modern healer, and a future shield

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The food microbiome, comprising microorganisms present in foods and fermentation, links diet, environment, and host physiology. This review examines its evolutionary, contemporary, and future nutritional relevance, including emerging applications of artificial intelligence (AI). In early human diets, fermentation likely improved food safety and nutrient accessibility, although its contribution to encephalization remains unproven. In modern populations, fermented foods and microbial metabolites shape the composition of the gut microbiome and modulate host metabolic, immune, and neuroactive functions. Rising atmospheric CO₂ is projected to reduce protein and micronutrient concentrations in staple crops, increasing interest in microbial fermentation as a strategy to enhance nutrient availability. Integration of AI with multi-omics enables functional characterisation of fermentation ecosystems and supports the development of targeted, personalised nutritional strategies, although translational and mechanistic challenges remain unresolved.

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Current Opinion in Biotechnology 2026, **100**:103555

This review comes from a themed issue on **Food Biotechnology**

Edited by **Yong-Su Jin** and **Soo Rin Kim**

Available online xxxx

<https://doi.org/10.1016/j.copbio.2026.103555>

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Introduction

Fermented foods carry complex microbiomes that enter the human gut; these communities and their metabolites bridge the environment, food, and host [1,2]. The food microbiome, the consortium of microorganisms we ingest and the fermented substrates they create, is often viewed through the narrow lens of preservation or flavour [2]. However, a broader temporal perspective reveals it as a primary driver of human biology. From the encephalization of *Homo* species to the impending nutritional crisis of the Anthropocene [3], the food microbiome represents a hidden lever of survival. This review highlights its role as an external digestive engine in the past, a regulator of homeostasis in the present, and a necessary shield against climate-induced malnutrition in the future. Food fermentation represents one of humanity's most transformative biotechnological innovations, fundamentally shaping the trajectory of human civilisation across millennia. The history of fermentation extends far deeper into our evolutionary past than previously recognised, emerging not merely as a response to nutritional necessity but as a catalyst for major shifts in human social organisation, dietary practices, and cognitive development. Understanding this evolution requires examining fermentation's role across multiple historical periods, from its prehistoric origins through to its crystallisation as an established practice in the 19th century. Food fermentation is one of humanity's most transformative biotechnological innovations, fundamentally shaping the trajectory of human civilisation over millennia [4]. Over the past two decades, fermented foods have regained considerable scientific, industrial, and consumer attention, transitioning from being valued primarily for preservation and flavour development to recognition as functional foods capable of delivering measurable physiological benefits. In parallel, recent advances in therapeutic probiotics show promising results across various health conditions, including gastrointestinal diseases, liver disorders, dermatological conditions, and mental health disorders [5]. Although not all fermented foods contain probiotics, many serve as important vehicles for the delivery of beneficial microorganisms and their metabolites, thereby contributing to their potential health-promoting effects. This shift reflects growing evidence that microorganisms possess

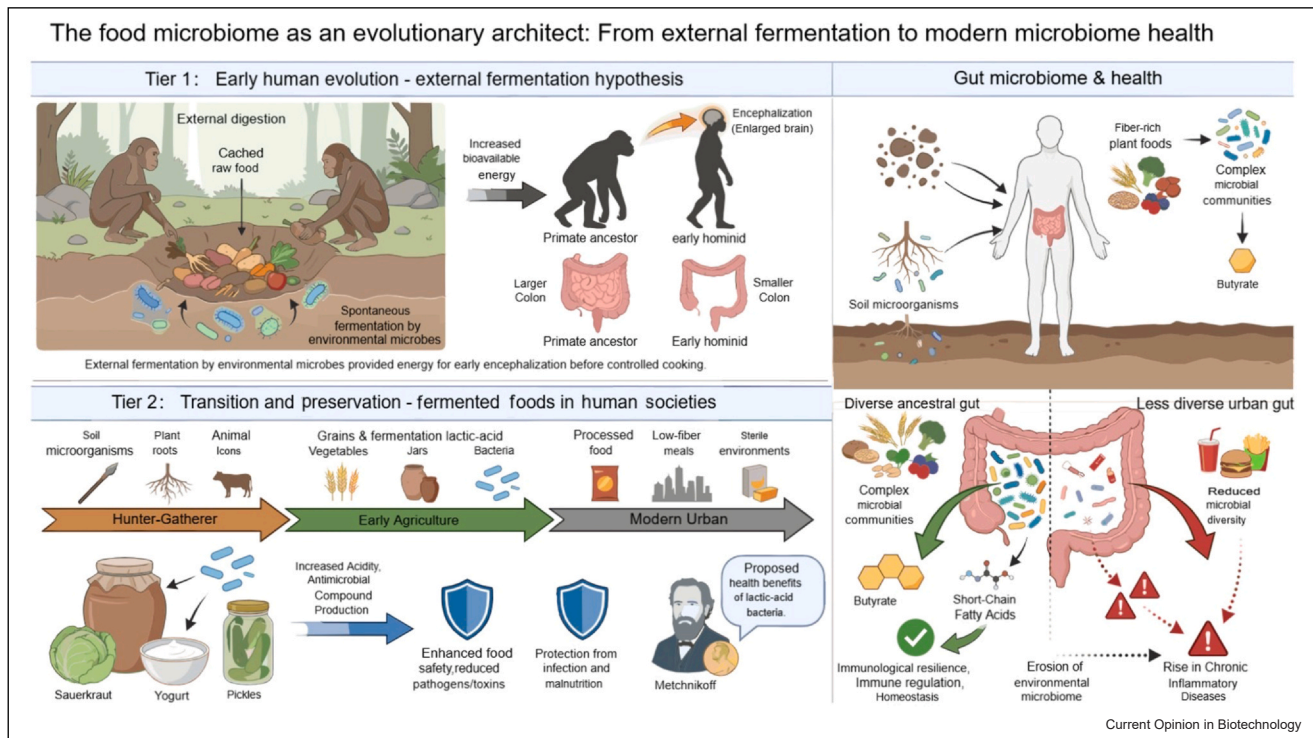
metabolic capabilities that complement plant-based fermented foods, including the synthesis of essential amino acids, the production of high-quality microbial protein, the improvement of bioaccessibility or bioavailability of minerals through enzymatic degradation of antinutritional compounds such as phytate, and the biosynthesis of vitamins. Through fermentation, microorganisms enhance micronutrient bioavailability, improving digestibility and boosting overall nutritional functionality [6]. The enhancement of nutritional and functional properties through fermentation extends across diverse food matrices and traditions globally, with precision-engineered fermentation biotechnologies now demonstrating reproducible improvements in both technological and health-relevant outcomes. Fermentation biotechnologies are increasingly regarded as central platforms for the development of functional foods, in which microbial metabolism generates bioactive compounds that may modulate host physiology, immunity, and metabolic homeostasis [7]. Multistrain starter cultures in sourdough systems have been shown to enhance both antioxidant capacity and rheological performance. The increased antioxidant activity may contribute to reducing oxidative stress markers in the intestinal microenvironment, while improved rheological performance enhances the overall quality of the dough and consumer acceptance, thereby promoting nutrient bioaccessibility and delivery [8]. Similarly, controlled fermentation of sausages using *Aspergillus niger* and *Lactiplantibacillus plantarum* starter cultures reshapes protein profiles and microstructure through enhanced proteolysis, releasing bioavailable peptides and amino acids that improve protein digestibility and nutritional quality. These tailored fermentation approaches are not limited to Western food systems. Traditional Asian plant-based solid-state fermentations, such as multistrain soybean fermentations involving *Bacillus* species, represent equally sophisticated microbial ecosystems that generate similar nutritional and functional improvements [9]. Beyond restoring nutrient composition, microbial metabolism during fermentation generates diverse bioactive compounds [10], which reach the host through two complementary pathways: (i) preformed metabolites present in the fermented food matrix (e.g. acetic and lactic acids, and extracellular peptides and other microbial metabolites generated during fermentation); and (ii) metabolites produced by viable microorganisms that survive gastrointestinal transit and remain metabolically active during their transient passage through the gut. Although these microorganisms generally do not establish permanent colonisation, they may temporarily integrate into the gut microbial community, where they interact with the resident microbiota and host tissues. This transient population provides a dynamic interface between dietary exposure and host physiology [5]. Together, fermentation-derived metabolites and viable microbial cells enable fermented foods

to influence gut microbial composition and metabolic activity. These complementary mechanisms provide a biological basis for the growing recognition of fermented foods as important components of modern nutrition and potential therapeutic applications. Elucidating food microbiome function requires moving beyond empirical observation toward experimental manipulation. Synthetic microbial communities (SynComs), artificially assembled consortia of defined microbial strains, provide this capability. Rather than studying complex natural fermentations containing 50–200+ species, SynComs reduce complexity to minimal, sufficient communities that preserve key functional properties [11]. This reductionist approach enables two critical advances: a mechanistic understanding of which strains generate specific metabolites, and the rational design of therapeutic microbial communities [11]. By moving from observation to controlled experimentation, SynComs transform the food microbiome from an evolutionary curiosity into a precision engineering framework.

The past: the food microbiome as an evolutionary architect

For decades, the ‘cooking hypothesis’ reigned as the primary explanation for the rapid increase in human brain size (encephalization). However, recent evidence suggests that the mastery of fire may have occurred later than the initial growth spurt of the hominid brain [12]. We argue that the ‘external fermentation hypothesis’ proposed by Bryant et al. [3] might offer the missing link. Before early humans could cook, they likely cached food. Spontaneous fermentation by environmental microorganisms served as a form of ‘external digestion’, breaking down complex macromolecules and increasing bioavailable energy without the metabolic cost of internal digestion (Figure 1). This provided the surplus energy required to fuel a metabolically expensive organ, the brain, while simultaneously supporting the reduction in colon size observed in modern humans [3]. The food microbiome was, in essence, our first biotechnology, unlocking the caloric density needed to transition from primate ancestors to intelligent hominids. Across the 20th and early 21st centuries, major gains in life expectancy have been largely attributable to sharp reductions in infectious disease and child mortality, driven by improvements in sanitation and access to safe water, vaccination, effective antimicrobial therapies, and broader maternal–child health and nutrition interventions, rather than to specific dietary changes [13]. Nevertheless, long before the microbial basis of disease was understood, fermented foods and beverages were widely used as preservation strategies: by increasing acidity and generating antimicrobial compounds, fermentation enhanced food safety, reduced exposure to foodborne pathogens, toxins and spoiling microorganisms, and helped protect populations from infection and

Figure 1



Evolutionary transitions in diet, food-associated microbes, and the human gut microbiome. Key stages linking dietary practices, food-associated microbial exposure, and gut microbiome function across human evolutionary and sociocultural transitions. **(a)** Early hominin food storage and environmental fermentation of plant substrates are proposed to increase nutrient accessibility and caloric yield, potentially contributing to metabolic adaptations associated with encephalization. **(b)** Traditional fermented foods illustrate the long-standing use of microbial fermentation, primarily by lactic acid bacteria, to preserve food, suppress pathogens, and generate bioactive metabolites before the formal recognition of microbial roles in disease and fermentation. **(c)** Hunter-gatherer dietary patterns, characterised by minimally processed, environmentally exposed foods, are associated with increased microbial exposure and greater gut microbiome diversity, factors linked to immune modulation and host-microbe co-adaptation. **(d)** The transition to agriculture and increasing food processing is associated with reduced dietary fibre and microbiota-accessible carbohydrates, dietary substrates that normally fuel microbial fermentation in the colon. **(e)** Industrialised Western diets, typically low in fibre and high in processed foods, are associated with reduced gut microbial diversity and altered microbial metabolism, including decreased production of SCFAs such as butyrate, metabolites involved in host metabolic and immune regulation. Abbreviations: SCFA, short-chain fatty acid; NCD, noncommunicable disease.

malnutrition [5]. Many of these fermentations are driven by lactic acid bacteria, a functional group of microorganisms commonly associated with traditional fermented foods. It was only in the early 20th century that Nobel laureate Ilya Mechnikov [14] proposed that these bacteria might beneficially modulate the intestinal microbiota, thereby promoting health and longevity, a hypothesis that remained speculative and lacked controlled experimental support at the time. The co-evolutionary relationship between humans and food-associated microbiota traces back to ancestral environments. Worth mentioning that spontaneous fermentation also carries inherent risks, including the accumulation of undesirable metabolites such as biogenic amines, mycotoxins, and other chemical hazards arising from uncontrolled microbial succession [15,16]. This limitation highlights the evolutionary trade-off between nutritional enhancement and microbial unpredictability and reinforces the modern need for controlled microbial ecosystems. By

replacing stochastic spontaneous succession with deterministic assembly through defined strain inoculation, SynComs systematically eliminate pathogenic and toxin-producing organisms while preserving fermentation's nutritional and functional benefits, representing a critical technological advancement over traditional methods.

Soil and plant microorganisms, to which humans were continuously exposed throughout evolutionary history, played a pivotal role in shaping the human gut microbiome and fostering immunological resilience [17]. Sustained ingestion of soil-contaminated plant materials and microbially rich foods during hunter-gatherer lifestyles drove the compositional and functional maturation of the gut microbiota, underpinning adaptive immune regulation [17]. Although the shift from hunter-gatherer to agricultural societies reshaped dietary profiles, microbially diverse foods and environmental exposures persisted as key ecological features across populations (Figure 1). Concurrently, urban dietary

patterns, characterised by high levels of food processing, low fibre intake, and reduced biodiversity, disrupt host–gut microbiome symbiosis, curtail microbial diversity, and impair metabolite-mediated immunometabolic signalling [18]. Declines in gut microbial α -diversity track urbanisation and global biodiversity loss, paralleling the epidemiologic rise of chronic noncommunicable inflammatory diseases in urban settings [17]. Westernised diets and diminished environmental microbial inputs further destabilise microbiota–host interactions, elevating susceptibility to metabolic and immune-mediated pathologies [18]. These convergent trends position the fermented food and environmental microbiome as an evolved buffer against immune dysregulation, wherein chronic exposure to microbial epitopes, short-chain fatty acids (SCFAs), and other immunomodulants preserved homeostasis; contemporary erosion of this interface likely exacerbates the inflammatory disease pandemic. Food components that were abundant in ancestral diets, particularly dietary fibre, remain central to microbiome health. Whole grains and fibre-rich plant foods sustained complex microbial communities capable of producing SCFAs, particularly butyrate, which serves as a crucial signalling molecule throughout the body [19]. The profile of digestible and indigestible carbohydrates determined nutritional quality, even in ancient times, with whole-grain sources providing indigestible dietary fibres that affected gut motility and supported beneficial microorganisms [19]. Modern SynCom reconstruction of spontaneous fermentations provides a novel lens for ancestral understanding. *De novo* reconstruction of sourdough synthetic communities reveals that dominant, subdominant, and satellite players together encoded the redundancy necessary for metabolic stability and resilience [20]. This modular architecture, rather than a single monolithic strain, characterises ancestral fermented foods. SynComs thus function as ‘functional time machines’, revealing which microbial players our ancestors unknowingly selected for, thereby generating bioactive compounds essential for immune development and metabolic innovation. Although already used in several food fermentations [21], SynComs still require considerations on meta-omics data rather than simply mixing selected strains for industrial scalability.

The present: the food microbiome as a modern healer

In the modern era, the role of the food microbiome has shifted from caloric amplification to homeostatic regulation. The industrialisation of diet has severed the ancestral stream of microbial inputs, contributing to the rise of noncommunicable diseases. The therapeutic potential of food-derived microorganisms has become increasingly evident through rigorous clinical investigation. Importantly, the microorganisms ingested through food that survive gastrointestinal transit and reach the colon may constitute a transient microbiome, whose composition depends on the nature of the exposure. This

transient population complements the resident gut microbiota and represents a dynamic interface between dietary choices and host physiology. The transient microbiome exerts long-term effects on host physiology predominantly through transient metabolite production (SCFAs, indole derivatives, secondary bile acids, LAB-derived metabolites), complemented by direct epithelial and immune cell signalling through microbial surface components, ecological modulation of resident microbiota composition and metabolic output, and epigenetic reprogramming of mucosal immune homeostasis. These mechanisms operate independently of permanent microbial colonisation, explaining why ingested microorganisms from fermented foods can confer measurable and sustained health benefits despite their transient presence in the gastrointestinal tract [22–24].

Fermented foods are a valuable source of novel probiotic strains enriched in nutrients and highly sustainable for the environment [5]. Recent advances in therapeutic probiotics have shown promising results across various health conditions, demonstrating the expanding understanding of how the human microbiome’s role in health and disease translates into clinical benefit [25]. Specific probiotic strains and combinations have demonstrated beneficial effects in gastrointestinal diseases, liver disorders, dermatological conditions, and even mental health disorders, reflecting the multilayered connections between the food microbiome and human physiology [25]. Postbiotics, defined as preparations of inanimate microorganisms and/or their components, including microbial metabolites produced during fermentation [26], have emerged as the next generation of biotherapeutics. These compounds, including SCFAs, antimicrobial peptides, and exopolysaccharides, positively impact gut health and modulate immune responses without the technological challenges associated with live probiotic cultures [27]. Heat-treated lactobacilli preparations (paraprobiotics) demonstrate bifidogenic effects, selectively promoting the growth of beneficial *Bifidobacterium* species in human faecal communities [28], offering a stable and scalable approach to microbiome modulation. Synbiotics, combinations of probiotics and prebiotics designed to enhance gut health, can complement postbiotics by promoting beneficial microorganisms and suppressing pathogens, further improving overall gut microbiota composition. The therapeutic applications of the food microbiome extend to the management of chronic diseases characterised by dysbiosis. Ultra-formulated foods, characterised by synthetic additives, low fibre content, and simple and refined sugars (syrups), are associated with decreased microbial diversity and reduced levels of beneficial bacteria. Conversely, dietary modifications incorporating fermented foods and prebiotics help mitigate these detrimental effects [29]. A core microbiome signature has been identified that serves as a holistic health indicator, with one guild

specialised in fibre fermentation and butyrate production and another characterised by virulence and antibiotic resistance [30]. This distinction provides a mechanistic framework for understanding how specific dietary interventions can shift the microbiota toward health-promoting configurations.

Current research underscores the diet-therapeutic potential of reintroducing diverse food microbiomes (e.g. fermented foods, synbiotics) to restore gut homeostasis. We are, indeed, witnessing a profound paradigm shift in how the food microbiome is understood and utilised in modern medicine. Single-strain probiotics show modest and variable efficacy, partly because the therapeutic power of natural fermentation derives from synergistic multispecies interactions. SynComs address this limitation through two complementary design strategies [11]. Bottom-up approaches select strains based on specific functional traits, nutrient production, pathogen inhibition, immunomodulation, then assemble minimal consortia [11]. Top-down approaches reconstruct simplified versions of natural fermented foods, identifying which dominant and subdominant members recapitulate original functionality [21]. The critical advantage is that SynComs reveal mechanistic interactions: how one strain's metabolite fuels another's growth, creating resilience impossible with single strains [21]. This rational design transforms fermented foods from undefined complex cultures into precision therapeutics, enabling standardised production and reproducible clinical outcomes. SynCom may function as adjuncts in starters, improving the potential of the inherent fermentation process, or as substitutes for original starters, thus stabilising or accelerating the industrial fermentation process [11,31]. The gut–brain axis, the bidirectional communication network between the gastrointestinal tract and the central nervous system, represents one of the most exciting frontiers in neuroscience and nutrition [32]. This communication occurs through multiple pathways, including the vagus nerve, immune signalling, and neuroactive metabolites produced by gut microorganisms [33]. Emerging evidence demonstrates that food-derived microorganisms and their metabolites can directly modulate cognitive function, emotional resilience, and stress response, fundamentally challenging the traditional separation between nutrition and psychiatry [32]. Psychobiotics, defined as live beneficial microorganisms that confer mental health benefits when administered in adequate amounts, represent a revolutionary therapeutic category emerging from this paradigm shift [33]. The vagus nerve, which directly connects the enteric nervous system to the brain, serves as a major conduit for microbial signals, transmitting information on microbial composition and metabolite production to neural centres that govern mood, memory, and stress responses [34]. This anatomical reality explains how dietary changes affecting microbiota

composition can produce measurable improvements in anxiety, depression, and cognitive function within days to weeks [34]. The mechanisms by which food microbiota influence mental health operate through several well-characterised neuroactive compounds. SCFAs, particularly butyrate, have emerged as critical mediators that cross the blood–brain barrier and directly regulate neurotransmitter synthesis, microglial function, and neuroinflammatory responses [35]. Butyrate enhances brain-derived neurotrophic factor (BDNF) expression, a crucial protein supporting synaptic plasticity, learning, and stress resilience [35]. In addition to SCFAs, gut bacteria can produce gamma-aminobutyric acid (GABA), a neuroactive metabolite that acts as the brain's primary inhibitory neurotransmitter, modulating neuronal excitability and contributing to stress and anxiety regulation, as well as influencing cognition, emotion, sleep quality, and systemic metabolic responses. Additionally, tryptophan-derived metabolites represent another critical pathway; specific bacterial metabolites, including kynurenine pathway products and indole derivatives, regulate immune cell differentiation, blood–brain barrier integrity, and anxiety-like behaviours [35]. The gut–brain axis operates bidirectionally; chronic stress and anxiety themselves alter microbiota composition toward dysbiosis, creating a vicious cycle that perpetuates mental health deterioration [18]. Breaking this cycle through dietary interventions that restore beneficial microbiota composition represents a practical, evidence-based approach to stress management and anxiety prevention [36]. This finding offers hope for individuals with treatment-resistant psychiatric conditions, suggesting that optimising the food microbiome through targeted nutrition may offer adjunctive benefits alongside or potentially as an alternative/completion to pharmacological interventions in select cases.

The future: the food microbiome as a future shield

Rising atmospheric CO₂ concentrations are altering plant physiology in ways that extend beyond productivity to affect nutritional quality. Although carbon fertilisation can increase biomass accumulation, it simultaneously reduces concentrations of protein and essential micronutrients, including iron and zinc, in major staple crops such as wheat, rice, and legumes [37]. This shift threatens to decouple caloric sufficiency from nutritional adequacy, creating a scenario in which food systems may provide sufficient energy yet fail to meet fundamental physiological requirements. As a result, nutrient insecurity may increase even where food availability remains stable, with important implications for global health [38]. These emerging constraints highlight the need for biological strategies to restore nutrient density in plant-based food systems. This requirement is further intensified by the growing consensus that a transition towards predominantly plant-based dietary patterns is

necessary to improve the environmental sustainability and resilience of global food systems. However, because plant nutritional quality is intrinsically sensitive to elevated CO₂ and constrained by lower bioavailability of key micronutrients, this transition may inadvertently amplify the risk of nutrient insufficiency, reinforcing the urgency of developing complementary biological solutions. The food microbiome, the microbial communities associated with fermented foods, provides a mechanistic and scalable strategy to address this challenge and is increasingly recognised as a critical component of next-generation food systems [6]. Microorganisms possess metabolic capabilities that complement plant physiology, including the synthesis of indispensable amino acids, the production of high-quality microbial protein, the liberation of minerals through enzymatic degradation of antinutritional compounds such as phytate, and the biosynthesis of vitamins. Through fermentation, microorganisms can convert nutritionally diluted plant substrates into biochemically enriched foods, partially compensating for CO₂-induced nutrient loss. These processes also enhance micronutrient bioavailability, improve digestibility, and boost overall nutritional functionality [10].

Beyond restoring nutrient composition, fermentation-associated microbial metabolism generates diverse bioactive compounds (SCFAs, bioactive peptides, and complex polysaccharides) that directly influence host physiology by regulating the immune function, metabolic homeostasis, and intestinal barrier integrity. The collective metabolic activity of fermentation ecosystems, emerging from the interacting microbial community, their collective genome, and associated metabolic networks, the so-called fermentome, constitutes the functional basis through which microorganisms transform raw substrates into physiologically active foods. Advances in artificial intelligence (AI) and multi-omics technologies now enable detailed characterisation of these processes and their integration with host biological data [39].

Rather than attempting to model 200+ interacting species computationally, SynComs of increasing complexity provide tractable training platforms for machine learning algorithms [11]. Functional predictability emerges from ecological organisation rather than or only from specific species composition. The minimal sufficient communities achievable through SynCom design enable AI systems to learn reproducible, mechanistically interpretable fermentation rules, thereby supporting the development of personalised, optimised fermentations that are responsive to individual microbiome composition and nutrient needs. Beyond microbiome composition analysis alone, comprehensive characterisation of fermented food quality and functional outcomes requires integration of objective instrumental metabolomics with advanced multivariate statistical analysis and machine learning. Metagenomics, metatranscriptomics, metaproteomics, and metabolomics can be systematically

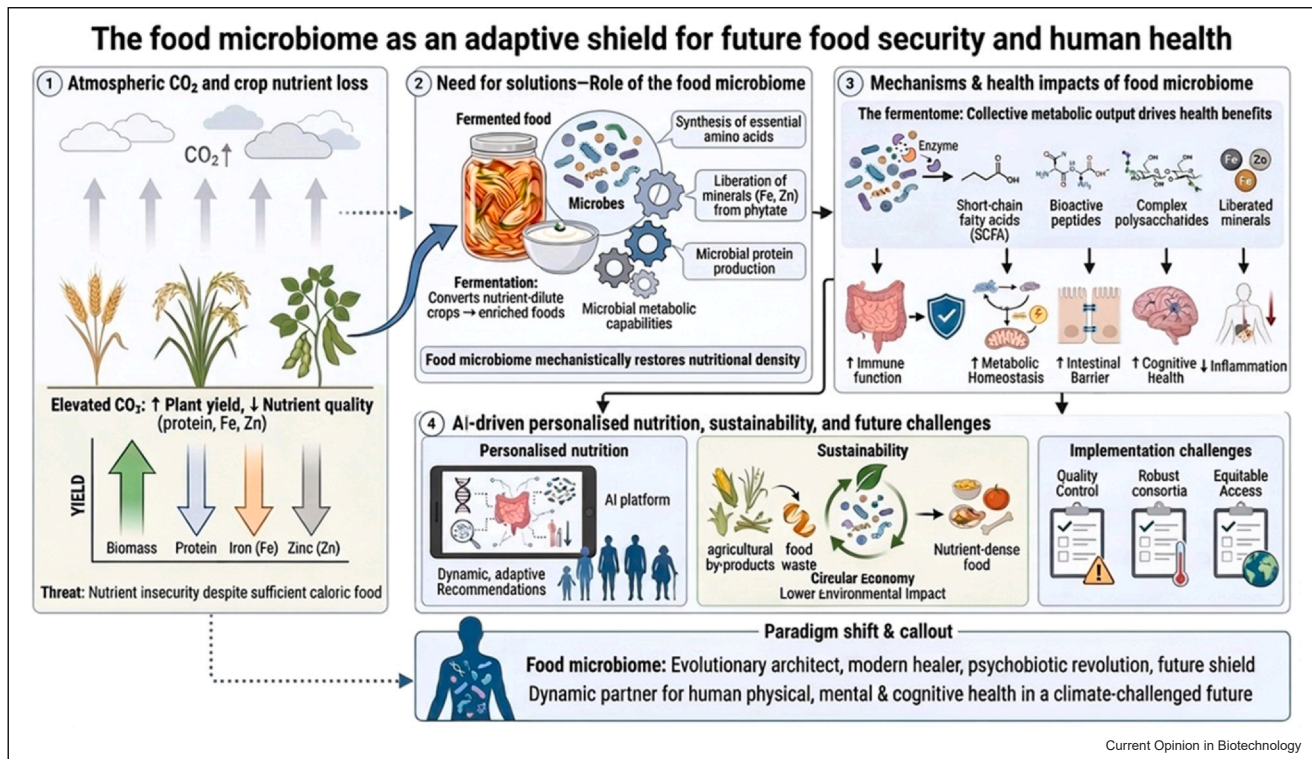
integrated to understand microbial function in fermented foods, with multi-omics data integrated into predictive safety and quality models to identify critical fermentation pathways and their impact on final product quality, enabling more precise control over fermentation processes and improving consistency.

Untargeted metabolomics using gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) platforms enables comprehensive identification of volatile and non-volatile metabolites across traditional fermented foods [40]. Subsequent multivariate statistical analysis, including principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA), and orthogonal partial least squares discriminant analysis (OPLS-DA) identifies key flavour markers and metabolite pathways, such as plant secondary metabolite biosynthesis and amino acid metabolism, directly linked to sensory quality, nutritional value, and regional differentiation across fermented food systems [40].

Additionally, electronic nose (e-nose), electronic tongue (e-tongue), and electronic eye (e-eye) technologies coupled with conventional analytical methods and multivariate analysis can monitor volatile compound dynamics during fermentation and storage, with correlation analysis establishing quantitative associations between environmental factors (pH, total acidity, nitrite), microbial community succession patterns, and specific aroma-active volatile compounds (esters, aldehydes, ketones, organic acids) that serve as predictive variables for fermentation stage advancement and product quality assessment during distribution and storage [41]. By systematically linking microbial succession data (metagenomics) to real-time metabolic output (untargeted metabolomics + electronic senses) and sensory properties (GC-MS flavoromics + electronic nose), multi-omics-guided strategies for SynCom design enable iterative optimisation through Assembly–Assessment–Redesign (A-A-R) workflows, where AI systems learn mechanistically interpretable rules governing fermentation performance and metabolite [42,43]. This multi-omics-informed approach, integrating metagenomics, metatranscriptomics, metaproteomics, metabolomics, and culturomics with machine learning, transforms fermentation from an empirical craft into a data-driven precision technology, enabling standardised production of fermented foods with targeted nutritional, sensory, and functional properties aligned with personalised consumer preferences and health objectives [43].

AI-enabled personalised nutrition platforms can incorporate microbiome composition, host genetics and metabolic biomarkers to generate adaptive dietary recommendations and guide the design of fermented foods with targeted functional properties [6,39] (Figure 2). Such approaches represent a shift from static, population-level dietary recommendations towards dynamic nutritional strategies

Figure 2



The food microbiome as a strategy to enhance nutritional quality and resilience in future food systems. Microbial fermentation and food-associated microbial communities may mitigate emerging nutritional challenges in modern food systems. Rising atmospheric CO₂ concentrations are associated with reduced protein and micronutrient densities in staple crops. Fermentation-driven microbial processes can enhance nutrient availability, generate bioactive metabolites, and improve micronutrient bioavailability, with potential implications for immune, metabolic, and cognitive health. Advances in artificial intelligence and multi-omics approaches enable the development of personalised nutrition strategies and targeted food design, supporting more resilient and sustainable plant-based dietary systems. Fermentation technologies may also contribute to circular food systems by valorising agricultural by-products and reducing waste streams. Remaining challenges include the standardisation of microbial consortia, the reproducibility of fermented products, and the establishment of causal links between microbial metabolites and human health outcomes.

tailored to individual biological characteristics. Intervention studies have demonstrated that personalised nutrition programmes incorporating microbiome-informed dietary modulation can increase microbial diversity, enrich beneficial taxa such as *Faecalibacterium*, and reduce proinflammatory microbial signatures, supporting their potential role in disease prevention and metabolic regulation [6].

These developments are particularly relevant in the context of ageing, where progressive alterations in microbiome composition contribute to systemic inflammation, metabolic dysfunction and declining immune resilience. Fermented foods enriched with specific microbial strains and metabolites have been associated with improvements in metabolic parameters, reduced inflammation, and enhanced immune function [44]. By modulating microbial ecosystem structure and metabolic output, personalised fermented foods may therefore support physiological resilience and complement conventional medical therapies across the lifespan. The

implications extend beyond individual health to the sustainability and equity of global food systems. Fermentation provides a cost-effective and energy-efficient method to improve food quality, safety and stability while enhancing nutritional value [5]. Microbial processes can convert agricultural by-products and food waste into nutritionally valuable foods, supporting circular economy models that reduce resource waste and environmental impact [45]. Through targeted microbial ecosystem design, fermentation enables the production of nutrient-dense foods with desirable sensory and functional properties without reliance on chemical fortification or resource-intensive processing (Figure 2).

Despite these advances, several challenges remain for large-scale implementation. Ensuring reproducibility and stability of microbial consortia, understanding which fraction of the food microbiome is actively transferred to the intestine, standardising fermentation processes and establishing robust quality control systems are essential

for consistent product performance [46]. Regulatory oversight and safety assessment, including evaluation of novel strains and metabolite profiles, will also be critical. In addition, integrating multi-omics datasets across diverse populations and establishing causal relationships between specific microbial metabolites and health outcomes requires further mechanistic and longitudinal investigation [46]. Addressing individual variability in microbiome composition, host genetics and probiotic responsiveness, alongside consumer acceptance, cost-effectiveness, and equitable access, will also be critical to ensure equitable and effective application of personalised nutrition strategies [47].

Conclusion

The food microbiome integrates evolutionary wisdom with contemporary science and future precision medicine. From its role in shaping human immune resilience across evolutionary time, to its current therapeutic applications in treating dysbiosis-related diseases, to its psychobiotic potential in revolutionising mental health care, and to its future promise in preventing chronic illness through personalised nutrition, the food microbiome represents a fundamental frontier in human health. A systematic framework integrating anatomy, physiology, immunology, and genetics reveals that humans are more accurately described as ‘meta-hosts’ that include symbiotic microorganisms as essential components of human health [47]. The practical translation of microbiome science requires addressing challenges in standardising research methodologies, considering individual variations in microbiome composition and host genetics, ensuring equitable access to personalised microbiome-based interventions, and recognising gender-specific differences in probiotic responses [36]. Future research must focus on longitudinal studies examining the long-term effects of specific dietary interventions, mechanistically driven investigations identifying causal relationships between microbiota changes and health outcomes, and multi-omics integration to understand the complex interactions governing microbiome function. Causality remains incompletely established; most human evidence is associative rather than causal, with limited randomised controlled trials, methodological heterogeneity, and variability in fermented food products and microbial strains. Substantial interindividual variability in microbiome composition, host genetics, and probiotic responsiveness constrains clinical utility; current predictive biomarkers for identifying responders remain underdeveloped. While metabolite production by the fermented food microbiota is well documented *in vitro*, the contribution of transient versus resident microorganisms to total metabolite production *in vivo* remains incompletely quantified. Fermented foods remain characterised by extraordinary variability in microbial composition and metabolite profiles depending on

substrate, environmental conditions, and fermentation duration. Most of the research on fermented foods originates from high-income Western populations, limiting its generalisability to diverse global populations with distinct dietary traditions and genetic backgrounds. Additionally, cost, infrastructure requirements for multi-omics profiling, and healthcare system integration pose substantial barriers to implementing personalised interventions at the population scale, particularly in low-resource settings. To advance the food microbiome toward implementable precision nutrition, the field must prioritise: (i) Standardisation: internationally agreed standards for fermented food characterisation, metabolite profiling, and quality control criteria; (ii) Mechanistically-driven clinical trials: prospective, adequately powered randomised controlled trials incorporating baseline microbiome profiling, multi-omics monitoring, and long-term follow-up to establish causality and identify responder populations; (iii) Precision nutrition implementation: AI-powered models integrating microbiome, genomic, and metabolic data for personalised fermented food recommendations; (iv) Global equity: expansion of research to underrepresented populations with culturally acceptable, locally relevant strategies; (v) Mechanistic clarity: causal inference methodologies establishing definitive relationships between specific microbial taxa, their metabolites, and health outcomes through transient microbe–host interaction mechanisms and metabolite-mediated pathways [48].

The food microbiome stands at the intersection of evolutionary biology, clinical medicine, nutritional science, psychiatry, and preventive healthcare. Its role as an evolutionary architect shaped human immunity and metabolism across millennia. Its current function as a modern healer demonstrates therapeutic potential across diverse chronic diseases. Its emerging role as a psychobiotic agent fundamentally transforms our understanding of mental health, revealing that anxiety, depression, and cognitive decline are partially tractable through dietary microbiome modulation. Its future promise as a shield against illness through personalised nutrition represents one of the most exciting frontiers in precision medicine. Bridging traditional fermentation knowledge with cutting-edge technology and AI-enhanced personalisation offers an unprecedented opportunity to leverage the food microbiome to optimise human health across all domains: physical, mental, and cognitive. As research continues to uncover the intricate mechanisms by which food-associated microorganisms influence human physiology through the gut–brain axis and metabolic pathways, the integration of microbiome science into clinical practice, mental health treatment protocols, and public health policy will likely become as fundamental to preventive medicine as vaccination and sanitation were to the twentieth century. The recognition that our food microbiome is simultaneously an

evolutionary architect, a modern healer, and a future shield marks a fundamental paradigm shift in how we understand food, health, and human potential. The food microbiome is not a static component of our diet; it is a dynamic partner that has shaped our past and is essential for our future. We evolved *because* of it, we stay healthy *with* it, and we will survive the climate crisis *through* it. As we face a future of compromised food systems, we must look to the microbial world not just for preservation, but for the preservation of humanity itself.

Author contributions

EZ: Conceptualisation, curation and writing the original draft. LN: review & editing. RdC: review & editing. MG: Conceptualisation and review. EK: Conceptualisation, review and editing.

Data Availability

No data were used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We acknowledge the financial support from Sapienza University of Rome, Grant number: B83C24007370005_Award Horizon Europe.

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- of special interest
- of outstanding interest

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Major findings: This recent study explores how fermentation can convert agricultural by-products and food waste into nutritionally valuable foods, supporting circular economy models that reduce resource waste and environmental impact while enhancing nutritional value. Importance: This work bridges sustainability concerns with nutritional enhancement, demonstrating that fermented foods are not only therapeutic for individual health but represent a practical solution to the global food security and climate challenges highlighted in your manuscript's 'future' section.

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