Customizing microbial protein to supply a sustainable solution for precision nutrition

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As the global demand for sustainable protein intensifies, microbial protein is emerging as a promising alternative to conventional protein sources. While current applications focus primarily on its use as an alternative protein resource, rapid advances in synthetic biology, metabolic engineering, and AI-guided design can potentially drive a shift toward the functional microbial protein tailored for individual dietary needs and health goals (precision nutrition). The development of such customized microbial protein is, therefore, gaining increasing attention. We propose that microbial protein, beyond its sustainability advantages, can serve as a modular nutritional chassis capable of delivering targeted health benefits, adaptive nutrient profiles, and responsive bioactivity. Unlocking this potential will not only expand the scope of food innovation but also reshape the future architecture of global food systems.

THE NUTRITIONAL ADVANTAGES OF MICROBIAL PROTEIN

The global food system is facing unprecedented challenges due to continuous population growth, intensifying climate change, and increasing resource constraints. Protein, an essential nutrient for human health, is in increasingly high demand that traditional production can barely keep pace.[1] In this context, microbial protein (MP) offers a promising solution to protein shortages and contributes to global food security and sustainable development. MP, which refers to biomass containing protein at a relatively high content, is derived from single-cell microorganisms, such as yeast, fungi, algae, and bacteria, by fermentation (Figure 1). MP is gaining increasing attention thanks to the rapid microbial growth on diverse and flexible feedstocks, minimal reliance on land and water, and high nutritional value.[2]

MP sources are characterized by exceptionally high protein content, ranging from 50–65% in bacteria, 29–65% in yeast, 40–60% in algal biomass, and 30–45% in fungal biomass, respectively.[2] More importantly, MP consists of all essential amino acids and may compensate for the deficiencies of plant proteins as the richness in lysine, threonine, and other amino acids that are commonly limited in plant-based sources. For example, yeasts' essential amino acid levels exceed FAO/WHO dietary requirements,[2] and bacterial MP source, *Clostridium autoethanogenum*, contains over 80% crude protein and has an amino acid profile comparable to fishmeal, making it attractive for aquafeeds.[3]

In addition to being a high-quality protein source, microbial biomass offers a diverse range of essential micronutrients that significantly enhance its nutritional value. Many MP sources are abundant in vitamins, particularly B-complex vitamins such as riboflavin, niacin, folate, and vitamin B6, which are crucial for energy metabolism and cellular function.[4] Yeasts, for example, also contain ergosterol, a precursor to vitamin D2 that can be activated through UV exposure, making them especially valuable for addressing vitamin deficiencies common in plant-based diets.[5] In addition to vitamins, microbial biomass naturally contains trace minerals such as iron, zinc, and selenium, which are essential for oxygen transport, enzymatic activity, immune defense, and antioxidant protection.[6] Importantly, these minerals exist in bioavailable organic forms (e.g., selenomethionine and selenocysteine in selenium-enriched yeast *S. cerevisiae*), improving their absorption and efficacy in both human and animal nutrition. Together, these components underscore the potential of MP as a nutrient-rich and multifunctional alternative to conventional protein sources, offering comprehensive nutritional benefits for both human and animal applications.

HEALTH-PROMOTING PROPERTIES OF MICROBIAL PROTEIN

Beyond serving as a high-quality protein source, MP offers remarkable functional benefits that further highlight its potential as a next-generation nutritional solution. One significant advantage lies in immune modulation. Various microalgae, including *Chlorella*, *Spirulina*, and *Haematococcus*, produce polysaccharides and phycobiliproteins capable of activating macrophages and lymphocytes, thus supporting both innate and adaptive immune defenses.[4] These compounds collectively enhance immune function and help mitigate excessive inflammatory responses in humans and animals. In terms of antioxidant defense, microbial biomass is naturally rich in potent antioxidant compounds. Microalgae synthesize a variety of natural antioxidants, such as carotenoids (e.g., β-carotene, lutein, and astaxanthin), which effectively scavenge free radicals. Notably, astaxanthin, a liposoluble carotenoid, exhibits antioxidant activity estimated to be 10 times higher than lutein and β-carotene and up to 100 times greater than α-tocopherol.[7] Additionally, yeast metabolites can also contribute to antioxidant defense; for instance, *Saccharomyces boulardii* produces glutathione, a key intracellular antioxidant.[8] By neutralizing reactive oxygen species, these microbial antioxidants help protect cellular lipids, proteins, and DNA from oxidative damage, thus reducing the risk factors associated with aging and chronic diseases. MP also supports gut health by promoting a balanced gastrointestinal microbiota and enhancing mucosal barrier function.[9] Moreover, dietary fiber derived from microbial cell walls—primarily in the form of β-glucans, mannans, and chitin—supports gut microbiota modulation, enhances intestinal barrier integrity, and contributes to systemic immune regulation. Collectively, the immune-enhancing and antioxidant properties of MP translate into effective disease prevention, potentially lowering the incidence of metabolic, infectious, and degenerative diseases in both humans and animals.

Consequently, microbial protein emerges as an indispensable solution to meet escalating global protein demands. As a valuable nutritional alternative, it offers high protein content, a balanced amino acid profile, abundant micronutrients, and bioactive properties—all produced through sustainable processes. As such, it represents a crucial component in securing future food and nutrition security.

POTENTIAL APPLICATION IN PRECISION NUTRITION

The future development of MP is expected to shift from general nutritional supplementation to customized precision nutrition—an emerging field that aims to tailor dietary interventions based on individual physiological states, genetic context, and health goals. This paradigm shift is additionally fueled by technological advancements in synthetic biotechnologies, including protein engineering and microbial strain engineering.

Designing engineered proteins for precision nutrition

Adjusting amino acid profiles to increase the levels of limiting essential amino acids, such as methionine and lysine, can help overcome deficiencies commonly associated with plant-based protein sources and provide a more complete and balanced amino acid supply. Additionally, MP can be engineered to incorporate functional proteins with inherent bioactivities, such as

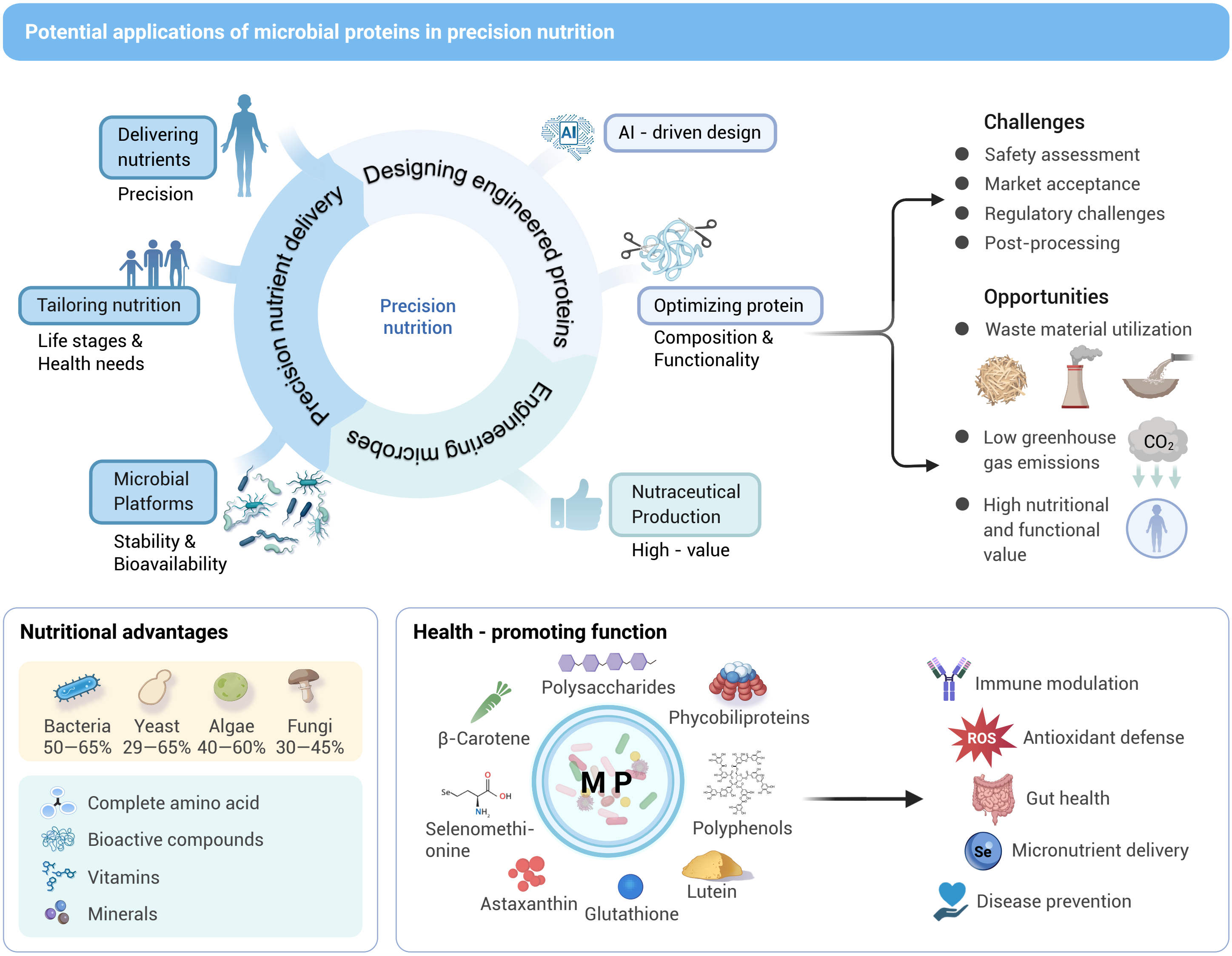

Figure 1. Overview of microbial protein highlighting its nutritional value, health-promoting properties, precision nutrition applications, and current challenges Microbial proteins (MPs) derived from bacteria, yeast, algae, and fungi are rich in protein, essential amino acids, vitamins, minerals, and dietary fiber. They exhibit health-promoting properties, including immune modulation, antioxidant activity, gut health support, and micronutrient delivery. With advances in AI and biotechnology, MPs can be integrated into precision nutrition strategies for various populations, as well as used in animal feed optimization. Despite challenges related to safety, regulation, and consumer acceptance, MPs represent a sustainable, low-emission alternative protein source with high nutritional and functional potential.

antimicrobial peptides and antiviral agents, enabling MP to act as both a nutritional source and a functional supplement that supports immune health and infection prevention.[2] A key direction lies in designing proteins with amino acid compositions and protein secondary structures for amino acid release at the desired rate and profile. In designing the protein with precisely defined structural and functional attributes, the integration of advanced computational design tools, including artificial intelligence algorithms (AlphaFold and MPNN, for instance), would be largely useful.[10] By understanding the relationship between sequence motifs and protease resistance, it becomes possible to engineer proteins with targeted digestion kinetics. Such proteins can be designed to release amino acids at specific rates, matching metabolic demands during different life stages, such as growth, pregnancy, or aging, or in clinical contexts where controlled nutrient delivery is critical for recovery and health maintenance.

Engineering microbes for high-value nutraceutical production

Further metabolic engineering strategies focus on modifying microbial metabolic pathways to enable the synthesis and accumulation of health-promoting compounds beyond proteins, such as polyunsaturated fatty acids (including DHA and EPA).[2] These compounds play crucial roles in cardiovascular health, cognitive function, and anti-inflammatory responses, greatly expanding the nutritional and therapeutic potential of MP. Additionally, engineered strains can be designed to produce high-value bioactive compounds, such as nutritional terpenoids, flavonoids, or sweet-tasting molecules, introducing entirely new functionalities or improving the taste and flavor of MP.

Leveraging integrated microbial platforms for precision nutrient delivery

Microbial cells can serve as effective nutrient delivery platforms. Engineered microbes are capable of secreting extracellular polymers or proteins that can selectively bind to and enrich specific micronutrients such as vitamins, minerals, and prebiotics, facilitating targeted and efficient nutrient supplementation.

MP also has the potential to act as a natural encapsulation system. Sensitive bioactive ingredients, such as polyphenols and ω-3 fatty acids, can be encapsulated within MP matrices to protect them from degradation during processing, storage, and gastrointestinal digestion, thereby enhancing their stability and bioavailability. This encapsulation strategy can improve the efficacy of nutrient delivery and allow for the controlled release of bioactive at specific sites within the digestive tract.

In summary, the programmable design of MP across protein sequence, metabolic, and delivery levels enables precision engineering, establishing a customizable platform for precision nutrition. This transition from generalized supplementation to targeted nutrition interventions will address critical global challenges, including nutrient supplementation and comprehensive health management in diverse biological systems.

CHALLENGES AND OPPORTUNITIES

As an emerging nutritional source, MP shows great promise for addressing global challenges driven by rapid population growth and increasing demands for sustainable food. However, its large-scale application faces critical challenges. Safety assessment remains a major concern, as food ingredients from unnatural microbes may introduce unforeseen allergens or toxic compounds. Customized MP products for food or supplements must undergo rigorous evaluations of pathogenicity, allergenicity, and potential toxin residues to ensure safety for human and animal consumption.

Market acceptance is another significant barrier. Many consumers perceive MP as less natural or safe than traditional proteins, limiting its broader application. Addressing this skepticism requires improving sensory qualities—such as taste, texture, and appearance—to meet consumer expectations. Post-processing of microbial biomass also presents technical challenges, including enhancing product stability, improving flavor, refining texture, and achieving an appealing appearance. Establishing comprehensive quality and safety standards is essential to build trust among consumers and regulators. Strict regulatory requirements further complicate MP development, involving complex approval processes that increase costs and delay market entry.

Despite these challenges, MP offers unique opportunities. Advances in microbial fermentation and metabolic engineering allow for efficient use of waste-derived carbon sources, reduced land and water use, and significantly lower greenhouse gas emissions, aligning with global sustainability goals. Microorganisms can convert low-cost carbon sources such as carbon monoxide, crop residues, and food processing wastewater into high-quality protein. For example, *Clostridium autoethanogenum* can utilize industrial CO emissions, reducing greenhouse gases and pollution.[3]

Currently, MP has achieved early industrial applications, including mycoprotein-based meat alternatives (Quorn) and animal feed ingredients like FeedKind® and SylPro®. Overall, with continued multidisciplinary collaboration and technological innovation, MP is well positioned to overcome challenges related to safety, cost, sensory properties, and regulation, paving the way for scalable, sustainable protein solutions to meet future nutritional needs.

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AUTHOR CONTRIBUTIONS

All authors contributed significantly to the development of this perspective. Weihe Rong was responsible for the conceptualization, drafting of the initial manuscript, and figure preparation. Xinru Wang contributed to the writing and figure design. Peng Xiao critically reviewed and edited the manuscript. Zhiguang Zhu provided supervision and contributed to manuscript revision. Guokun Wang provided overall supervision, project coordination, and contributed to the critical review and final editing of the manuscript. All authors contributed to the manuscript and approved the final version.

DECLARATION OF INTERESTS

The authors declare no competing interests.