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Review

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Harnessing chemical communication in plant–microbiome and intra-microbiome interactions

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Abstract: Chemical communication in plant–microbiome and intra-microbiome interactions weaves a complex network, critically shaping ecosystem stability and agricultural productivity. This non-contact interaction is driven by small-molecule signals that orchestrate crosstalk dynamics and beneficial association. Plants leverage these signals to distinguish between pathogens and beneficial microbes, dynamically modulate immune responses, and secrete exudates to recruit a beneficial microbiome, while microbes in turn influence plant nutrient acquisition and stress resilience. Such bidirectional chemical dialogues underpin nutrient cycling, co-evolution, microbiome assembly, and plant resistance. However, knowledge gaps persist regarding validating the key molecules involved in plant–microbe interactions. Interpreting chemical communication requires multi-omics integration to predict key information, genome editing and click chemistry to verify the function of biomolecules, and artificial intelligence (AI) models to improve resolution and accuracy. This review helps advance the understanding of chemical communication and provides theoretical support for agriculture to cope with food insecurity and climate challenges.

Key words: Plant–microbiome interaction; Intra-microbiome interaction; Chemical communication; Click chemistry; Genome editing; Artificial intelligence (AI)

1 Introduction

In nature, plants are colonized by microbes and inevitably interact with them (Matsumoto et al., 2022; Wang and Cernava, 2023). The microbiome is considered the "second plant genome," affecting plant nutrient absorption and resistance (Bordenstein and Theis, 2015; Srivastava et al., 2025). Investigating plant–microbiome and intra-microbiome interactions is thus critical for maintaining ecosystem stability, enhancing agricultural productivity, and ensuring global food security (Wang and Cernava, 2020; Lv et al., 2023).

Chemical language-mediated interactions are prevalent in plant–microbiome and intra-microbiome interactions (Xu et al., 2022; Zhou et al., 2022). Small molecules, particularly diverse metabolites secreted by plants and microbes, have been well-characterized as chemical languages (Cheng et al., 2025). Through these molecules, plants and microbes establish intricate communication networks, engaging in "secret conversations" that determine the outcomes of their interactions, ranging from mutualistic symbiosis to pathogenic invasions, and even the restructuring of entire microbial communities (Bordenstein and Theis, 2015; Srivastava et al., 2025). Microbes release small molecules (e.g., secondary metabolites) to achieve intra-kingdom and extra-kingdom interactions (Atkinson

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et al., 2013; Weiland-Bräuer, 2021). In turn, plants also secrete small molecules to communicate with microbes (Matsumoto et al., 2022; Pantigoso et al., 2022; Hacquard and Martin, 2024; Zhan and Wang, 2024). Through such complex chemical communication, plants alleviate harm from abiotic or biotic stress and benefit from regulated reciprocal symbioses with desired microbes (Lv et al., 2023; Hu et al., 2024). However, the molecular principles underlying plant recognition and differentiation of chemical signals, microbial responses to plant-derived metabolites, and the establishment of functionally bidirectional communication remain poorly understood. Insight into these chemical signaling events is key to understanding the emergent properties of plant–microbiome and intra-microbiome interactions (Fig. 1).

Aiming to address the limited understanding of chemical communication, we propose an interdisciplinary research framework as an addition to conventional methods. By integrating multi-omics (Wang et al., 2024), genome editing (Zhan et al., 2022), click chemistry (Chen MM et al., 2024), and artificial intelligence (AI) (Li et al., 2023; Zhao et al., 2023) (Fig. 2), we provide a new opportunity to enhance agricultural productivity and food security via effectively harnessing the potential of engineering chemical communication in plant–microbiome and intra-microbiome interactions.

2 Intra-microbiome and plant–microbiome interactions

Various intra-microbiome interactions, such as bacteria–bacteria, fungi–fungi, and fungi–bacteria interactions, take place in an ever-changing environment (Weiland-Bräuer, 2021) (Fig. 1). The chemical molecules in these ubiquitous interactions critically shape the microbial communities and exert profound effects on phytophysiological processes (Trivedi et al., 2020). Parallel to this, research into plant–microbiome interactions, encompassing plant-mediated recruitment of microbes, microbial modulation of plant physiology, and bidirectional signaling cascades, has deepened our understanding of these ecological dynamics (Xu et al., 2023; Srivastava et al., 2025). These advances in both intra-microbiome crosstalk and plant–microbiome interactions provide a foundational framework for dissecting the chemical communication networks that underpin these relationships, while highlighting key gaps and future directions in the field.

2.1 Microbe–microbe interaction

2.1.1 Bacteria–bacteria interaction

Bacteria–bacteria interactions represent a major component in the microbiome, shaping community assembly and functionality across diverse ecosystems (Hibbing et al., 2010). Chemical communication is pivotal in that process, facilitated by diverse molecular signals, including quorum-sensing (QS) molecules, toxins, and other secondary metabolites (Fig. 1a).

This chemical communication regulates the bacterial community dynamics by mediating cooperation and antagonistic competition (Fig. 1a). As the primary signaling system for bacterial communication, QS facilitates signal transduction through specific molecules, such as acyl-homoserine lactones (AHLs) (Zhang et al., 2012), autoinducing peptides (AIPs) (Wang et al., 2015), and autoinducer-2 (AI-2) (Brackman and Coenye, 2015). Although current research suggests that QS molecules are involved in pathogenic signaling (Wu and Luo, 2021), non-pathogenic bacteria can also secrete QS molecules, highlighting the need to re-examine and redefine the role of QS in bacterial interactions (Gu et al., 2021). Studies on bacterial competition have focused on interspecies competition. *Bacillus velezensis* produces iturins that play dual roles in antibiosis and biofilm disruption, directly suppressing the ability of the pathogen *Xanthomonas oryzae* to infect rice (*Oryza sativa* L.) (Jin et al., 2020). The seed endophyte *Sphingomonas melonis* in rice confers resistance against the pathogen *Burkholderia plantarii* by producing anthranilic acid, which inhibits the sigma factor RpoS and suppresses the biosynthesis of the toxin tropolone (TR) (Matsumoto et al., 2021). Competition among bacteria occurs not only between species but also within species (Paquette et al., 2018). Intraspecific competition among bacteria has attracted increasing attention in recent years (Ashrafi et al., 2017).

Research on bacterial cooperation has gained increasing interest over the past decade, although it still lags behind research on bacterial competition. *Escherichia coli* uses conjugation (e.g., F-plasmid transfer)

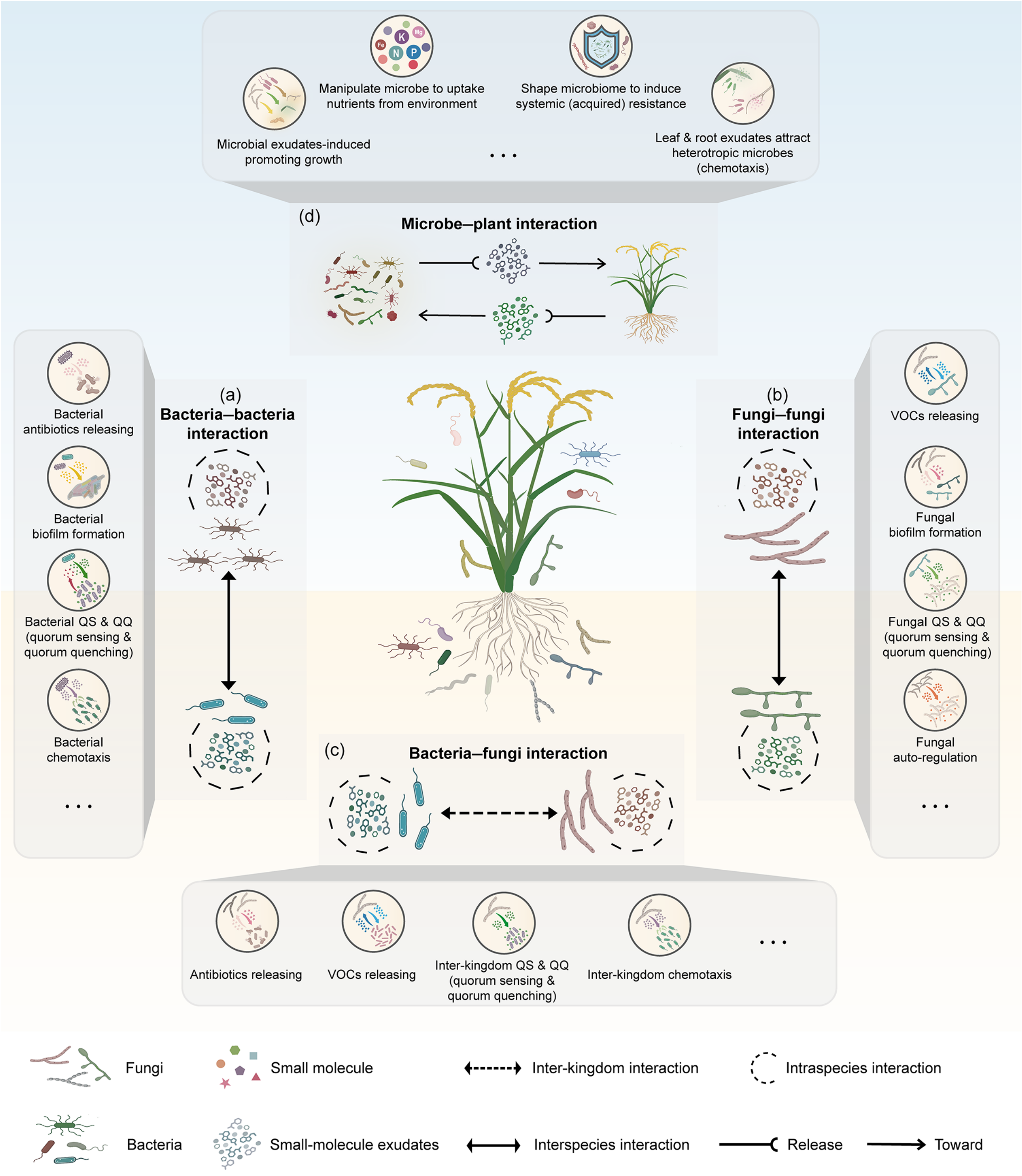

Fig. 1 Plant–microbiome and intra-microbiome interactions through chemical communication. Most of the binary chemical communications are in the forms of bacteria–bacteria (a), fungi–fungi (b), bacteria–fungi (c), and microbe–plant (d), forming plant–microbiome and intra-microbiome interactions. Mutualism, competition, and antagonism occur through the interactions among small chemical molecules of plants and microbes (such as antibiotics, quorum-sensing (QS) signals, and volatile organic compounds (VOCs)). Created in BioRender. Hongda, F. (2025) https://BioRender.com/iscmu2z

and intra-colony channels to adapt to environmental change and stress (Rooney et al., 2020). *Pseudomonas* and *Paenibacillus* exhibit synergistic defense against *Dictyostelium discoideum* through the exchange and modification of metabolites (Zhang et al., 2021). However, the chemical molecules involved in bacterial cooperation have rarely been studied, representing a gap in bacterial chemical communication.

2.1.2 Fungi–fungi interaction

Fungi–fungi interactions are important to the microbiome, driving community stability and ecological functional expression through chemical communication. Fungi, like bacteria, dynamically regulate cooperative, symbiotic, and competitive behaviors by releasing chemical signals (Dullah et al., 2021) (Fig. 1b).

Fungal autoregulatory mechanisms are indispensable in keeping the dynamic balance of inter-fungal interaction (Ugalde, 2006). Autoregulation through metabolic reprogramming enables fungi to preserve homeostasis under environmental fluctuations or interspecies competition (Fig. 1b). Branched-chain amino acids (BCAAs) and derivatives like 2-methyl-1-butanol act as QS molecules in *Ophiostoma ulmi*, inducing the mycelium-to-yeast transition under high inoculation density (Berrocal et al., 2012), though the underlying regulatory pathways remain unclear. A recent study shows that 3-octanol inhibits the growth and pathogenicity of *Botrytis cinerea* by inducing autophagy, upregulating *B. cinerea* autophagy-related (*BcATG*) genes, and suppressing spore germination-related genes (*B. cinerea* germination-related factor coding gene (*BcCGF1*), *B. cinerea* small GTPase coding gene (*BcCdc42*), and the mitogen-activated protein kinase coding gene (*BMP1*)) (Zhang et al., 2023). However, research on fungal chemical autoregulation in crop pathogens remains a significant knowledge gap.

Beyond self-regulatory mechanisms, inter-fungal interactions form complex biological interaction networks. *Aspergillus cvjetkovicii* can secrete 2,4-di-tert-butylphenol (2,4-DTBP) to neutralize the reactive oxygen species (ROS)-dependent pathogenicity of the pathogen *Rhizoctonia solani* in the phyllosphere of rice (Fan et al., 2024). Although 2,4-DTBP production by *A. cvjetkovicii* has been confirmed, it remains unknown whether it is produced independently or influenced by host plants and other microbes. Cocultivating the endophytic fungus *Epicoccum dendrobii* with *Aspergillus nidulans* and other filamentous fungi triggers widespread alterations in secondary metabolite synthesis (Wang et al., 2022). While the partial loss-of-function VeA1 protein activates silent gene clusters, the exact chemical signals driving these fungal interactions remain unclear.

2.1.3 Bacteria–fungi interaction

Environmental microbiomes are largely shaped by bacteria–fungi interactions, whose diversity is crucial for ecosystem stability and functionality (Zhou et al., 2022), leading to multilateral mutualism, competition, and antagonism. These interactions are mediated by the secretion of bioactive molecules (Fig. 1c).

Fungi and bacteria reciprocally regulate each other's physiological behaviors and metabolic pathways through mutual secretion of metabolites, mediated by antagonistic or competitive interactions (Fig. 1c). Bacteria such as *Pseudomonas chlororaphis* ZJU60 secrete phenazine-1-carboxamide (PCN), which disrupts fungal histone acetylation and inhibits mycotoxin biosynthesis in *Fusarium graminearum* (Chen et al., 2018). Volatile organic compounds (VOCs) from *Alcaligenes faecalis* N1-4 inhibit the growth and toxin synthesis of *Aspergillus flavus* (Gong et al., 2019), offering a novel biological solution for using agricultural products to control fungal and toxin contamination. Similarly, *Pseudomonas aeruginosa* produces the QS molecule 3-oxo-C12 homoserine lactone (3-oxo-C12-HSL) to regulate the virulence of *Candida albicans* by suppressing its yeast-to-hyphae transition (Hogan et al., 2004). Note that although many studies have shown that bacteria–fungi interactions affect pathogens, it remains unresolved how pathogens perceive metabolites and whether specific receptors are involved in mediating the signal transduction.

Antagonistic or competitive interaction has been well researched, but few studies have focused on beneficial interactions. Likewise, researchers have established a stable system through artificial implantation, such as successfully introducing the bacterium *Mycetohabitans rhizoxinica* into the filamentous fungus *Rhizopus microspores* (Giger et al., 2024), but the forms existing in nature and their functional roles await further investigation. This mutually beneficial relationship provides a new approach to the prevention and control of plant diseases.

2.2 Plant–microbe interaction

Plant–microbe interaction is an interdisciplinary field of microbial ecology and plant biology, with recent advances in molecular mechanisms, ecological functions, and applied technologies. The interactions between pathogens and plants have been extensively studied, mainly involving the pathogen-associated molecular pattern (PAMP)-triggered immunity (PTI) and effector-triggered immunity (ETI) mechanisms (Jones et al., 2024). Compared to classical plant–pathogen interactions, plant–microbe bidirectional regulation is gaining more interest. Microbes directly promote plant root development, nutrient acquisition, and stress resilience through the secretion of molecules (Luo et al., 2025) or indirectly protect plant health by suppressing pathogens (Lv et al., 2023). Contrariwise, plants manipulate root exudates and leaf secretions to recruit specific microbes and shape the microbiome (Su et al., 2024) (Fig. 1d).

Although many studies have elucidated some chemical molecular mechanisms, significant unresolved questions exist in plant–microbiome and intra-microbiome interactions, particularly in the recognition of microbe-derived small molecules by plants and vice versa. The detailed mechanisms by which plants sense and respond to small molecules released by microbes are an area that deserves intensive research (Cheng et al., 2025). Many studies have shown that plants recognize microbe-derived compounds (Fig. 1d). A plasma membrane lectin receptor-like kinase of *Arabidopsis*, resistant to DFPM-inhibition of abscisic acid signaling 2 (RDA2) receptor, detects microbial 9-methyl sphingoid base (derived from *Phytophthora ceramide* via an *Arabidopsis* apoplastic ceramidase, neutral ceramidase 2 (NCER2) cleavage) to trigger immune responses. Likewise, loss of RDA2/NCER2 compromises resistance, revealing lipid-mediated recognition mechanisms in plant defense (Kato et al., 2022). However, relatively few studies have researched the signaling cascades generated by specific receptors that modulate interactions (Trivedi et al., 2020), such as the underlying signaling pathways that link root responses to changes in the whole plant.

Although some nutrient exchanges have been discovered (Srivastava et al., 2025), understanding how microbes decode plant-derived molecular signals is a significant challenge in the field. Plant exudates play a crucial role in dynamically reshaping the microbiome (Fig. 1d). Studies have shown that rice maintains the homeostasis of the phyllosphere microbiome through secondary metabolite biosynthesis-related genes (Liu et al., 2023) (Fig. 1d). The *O. sativa* phenylalanine ammonia-lyase 02 (*OsPAL02*) gene of rice synthesizes 4-hydroxycinnamic acid (4-HCA) and enriches *Pseudomonadales* to balance the microbial community in the phyllosphere (Su et al., 2024). In these studies, genes that modulate the plant microbiome were designated “M genes” (Zhan and Wang, 2024). Uncovering how microbial receptors perceive plant signals could facilitate the breeding of disease-resistant crops by manipulating M genes.

3 Interdisciplinary approaches for harnessing unseen chemical communication

Various technologies have been developed to explore key clues and clarify the specific mechanisms of plant–microbiome and intra-microbiome interactions. Microbial screening, culturing, and chromatography-mass spectrometry are classical investigative approaches that can help reveal some preliminary signals. However, the absence of proper integration methods has led to limitations in the deeper analysis of mechanisms (Sharma et al., 2020).

The emergence of advanced technologies has invigorated the field and offers unparalleled opportunities and breakthroughs in investigating plant–microbiome and intra-microbiome chemical communications (Hussain et al., 2023; Hanif et al., 2024; Lasch et al., 2025). We have designed a technical framework that uses multi-omics integration for data analysis and prediction, genome editing and click chemistry to verify chemical communication from different angles, and AI to support the framework’s feasibility, accuracy, and efficiency (Fig. 2).

3.1 Multi-omics integration

The basis for exploring chemical communication lies in detecting the molecules involved and understanding how they are perceived by the responders. As a systematic approach that combines omics data (e.g., genomics, transcriptomics, proteomics, metabolomics, and microbiomics), multi-omics integration enables the identification of key functional genes, molecules, and microbes (Zhan et al., 2022) (Fig. 2a). It also promotes the design of synthetic microbial communities (SynComs) and the stabilization of the natural microbiome via small molecules, optimizing inter-kingdom metabolite exchange to enhance plant stress resistance (Tariq et al., 2025).

Multi-omics integration is valuable in chemical communication research. Su et al. (2024) integrated

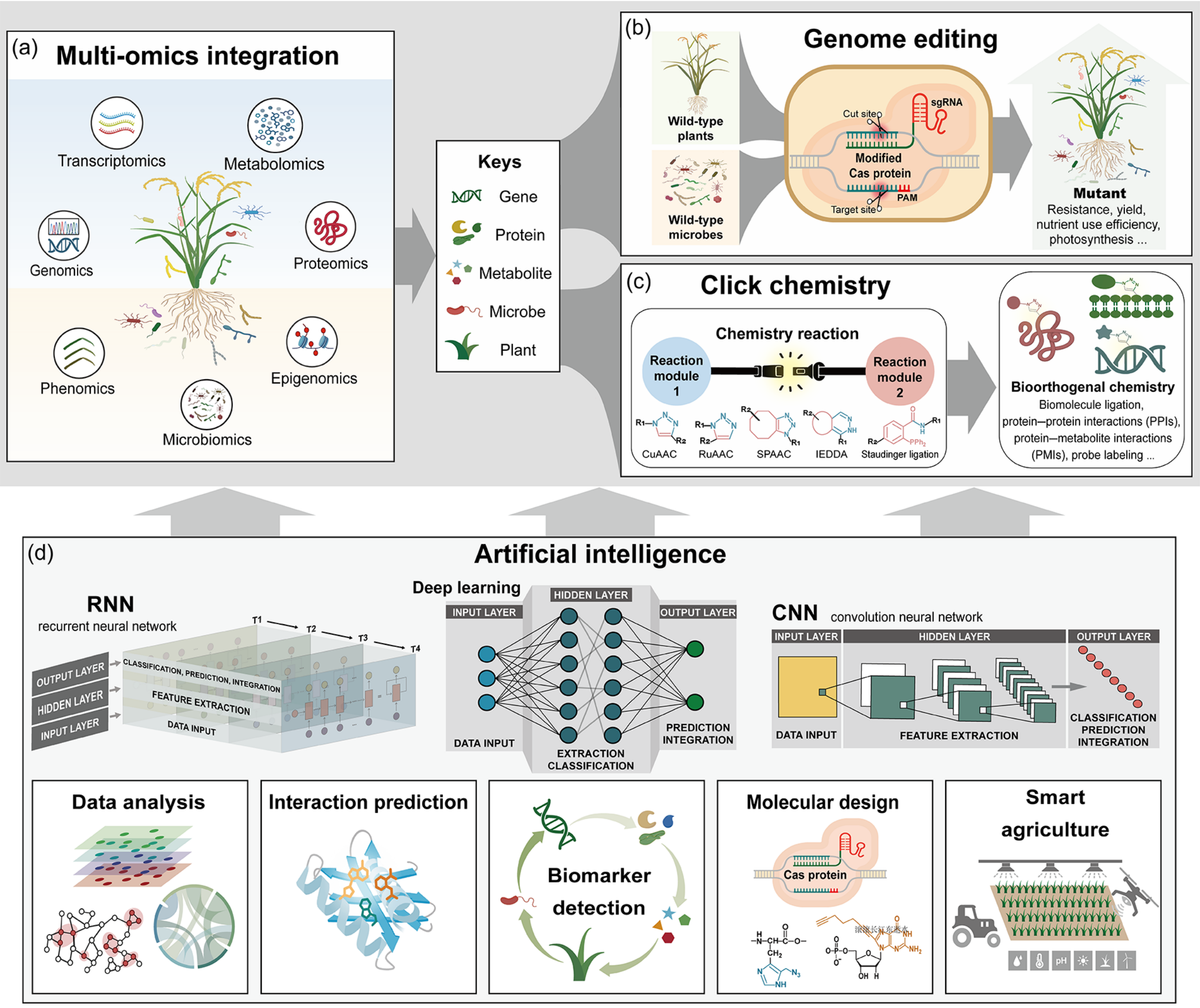

Fig. 2 Holistic engineering framework revealing chemical communication in plant–microbiome and intra-microbiome interactions. (a) Multi-dimensional data are analyzed through multi-omics integration (such as microbiome, genome, and transcriptome) to predict key factors. (b) Genome editing technology involves modifying genes for metabolism and signal sensing and developing plants and microbes with specific functions to verify key information at the gene level. (c) Click chemistry enables real-time labeling and tracking of biomolecules in situ, analyzing chemical communication at the metabolite level. (d) Artificial intelligence (AI) is applied in information analysis and plant–microbiome and intra-microbiome interaction prediction, biomarker detection, molecular design, and chemical communication result applications through smart agriculture (d). Cas: clustered regularly interspaced short palindromic repeats (CRISPR)-associated protein; CuAAC: copper-catalyzed azide–alkyne cycloaddition; IEDDA: inverse electron demand Diels-Alder reaction; PAM: protospacer adjacent motif; RuAAC: ruthenium-catalyzed azide–alkyne cycloaddition; sgRNA: single-guide RNA; SPAAC: strain-promoted azide–alkyne cycloaddition. Created in BioRender. Hongda, F. (2025) https://BioRender.com/2ohvpic

Genome-wide Association Study (GWAS) and metabolomics to demonstrate that the rice *OsPAL02* gene regulates the biosynthesis of 4-HCA, which selectively enriches beneficial *Pseudomonadales* to inhibit the growth of pathogen *X. oryzae*. In addition, the integration of microbial, metabolomic, and transcriptomic data showed that the core microbiome of the rice panicle (e.g., *Lactobacillus* spp. and *Aspergillus* spp.) suppresses infection by *Ustilaginoidea virens* through a BCAA-mediated defense mechanism (Liu et al., 2023). These examples demonstrate the advantages of multi-omics integration in locating key factors such as genes, microbes, and secondary metabolites in chemical communication. Multi-omics integration in plant microbiome studies faces challenges, such as heterogeneity across omics layers, which hinders the interpretation and resolution of the framework. Data processing and algorithm development and standardization remain critical for robust multi-omics integration, and multi-omics data analysis based on AI is needed (Kimotho and Maina, 2024).

3.2 Genome editing

After key information is mined through multi-omics integration, genome editing is generally required to verify the specific functions of genes, proteins, microbes, and metabolites. Genome editing can precisely manipulate genes involved in metabolite synthesis, perception, and regulation (Fig. 2b). This technology not only analyzes the chemical communication network at the genetic level, but also paves the way for breeding functional crops that enrich beneficial microbes, thereby contributing to sustainable food production under global environmental pressures (Zhan et al., 2022).

As an indispensable tool in plant microbiome research, genome editing is increasingly being adopted for exploring plant–microbiome and intra-microbiome interactions. In *Marchantia paleacea*, editing the genes of a pair of lysM receptor-like kinases, *MpaLYR* and *MpaCERK1*, demonstrated their dual roles in balancing symbiosis and immunity through chitin oligomer signaling (Tan et al., 2025). Emerging genome editing tools (base/prime editors) and nanoparticle-mediated delivery systems enabling precise single-nucleotide substitutions are also used. Traditional genome editing techniques are insufficient to support the study of chemical communication (Li BS et al., 2024). Cas proteins and guide RNA (gRNA) designed by AI can enhance the specificity of genome editing (Callaway, 2024, 2025) and have greatly increased its ability to reveal complex signaling networks (Fig. 2b).

Nevertheless, genome editing faces technical and regulatory barriers, such as inefficient delivery in recalcitrant tissues and off-target effects in polyploid crops, both of which remain critical bottlenecks (Li BS et al., 2024). Current challenges include transformation and regeneration protocols, low efficiency of homology-directed repair (HDR), and multigenic regulation of complex traits (e.g., quantitative trait loci (QTLs)) (Gao, 2021).

3.3 Click chemistry

To verify the functions of key compounds more intuitively and efficiently, click chemistry serves as an efficient tool to analyze chemical communication at the metabolite level. Click chemistry enables rapid and efficient synthesis of compounds by splicing them into small units. Its advantages include mild reaction conditions, high yield, good selectivity, and compatibility with biological systems. A key development in click chemistry is copper-catalyzed azide–alkyne cycloaddition (CuAAC) (Kolb et al., 2001). Strain-promoted azide–alkyne cycloaddition (SPAAC) has become a milestone in bioorthogonal chemistry (Sletten and Bertozzi, 2011) (Fig. 2c).

In plant–microbiome and intra-microbiome interactions, click chemistry can trace chemical molecules by labeling them with azide and alkyne clickable groups for detection. Morimoto et al. (2022) synthesized a clickable probe, DK-01, carrying an alkyne mini-tag and a photoreactive benzophenone group to analyze tobacco-secreted PRp27 during bacterial infection, revealing that its overexpression inhibits pathogen growth and enhances plant immunity. Maierhaba et al. (2024) used dual bio-orthogonal non-canonical amino acid tagging (Dual-BONCAT) to apply two clickable amino acid analogues (non-canonical amino acids (NCAAs)) to salt marsh microbes, detecting day-active *Methylobacterium* and night sulfur-cyclers by imaging and sequencing while reducing cross-experiment variability. Click chemistry also aids in identifying receptor proteins that recognize chemical signaling through mass spectrometry (Bishnoi et al., 2025) (Fig. 2c).

However, click chemistry has limitations in adaptability and stability within biological systems, and its application in studying biomolecule activities requires precise optimization (Chen MM et al., 2024; Whidbey, 2025). Using AI to design clickable probe molecules may help improve the specificity and high-throughput reaction capabilities of click chemistry (Chen et al., 2023; Zhu et al., 2024). Future development of AI-guided probe design will further expand the applicability of click chemistry in plant systems.

3.4 Artificial intelligence

AI offers transformative advantages over conventional methods in omics analysis by addressing critical limitations such as data heterogeneity, dimensional complexity, and low signal-to-noise ratio (Cembrowska-Lech et al., 2023; Gandomi et al., 2023). AI models like machine learning (ML) and deep learning (DL) use clustering and dimensionality reduction methods to extract hierarchical features from noisy, unstructured multi-omics data and enable accurate prediction from hidden patterns and non-linear relationships (Zhao et al., 2023; Bai et al., 2024). These capabilities can streamline labor-intensive preprocessing steps like feature selection and normalization, thereby facilitating biomarker discovery and function prediction (Cembrowska-Lech et al., 2023; Zhao et al., 2023) (Fig. 2d). For example, Chen SS et al. (2024) established a model named rice bakanae disease-visual geometry group (RBD-VGG) to enable early, non-destructive detection of disease. This DL model achieved high accuracy by analyzing hyperspectral and phenotypic data, significantly outperforming traditional visual inspections and molecular techniques.

AI models can also design specific proteins and molecular probes for genome editing and click chemistry based on previous prediction results. DL-based structure prediction and generation models, such as AlphaFold, enable atomic-resolution protein design (Jumper et al., 2021), thereby enhancing the targeting and efficiency of verification experiments in genome editing. Li JB et al. (2024) developed clustered regularly interspaced short palindromic repeats (CRISPR)-associated protein 9 (Cas9) variants with better specificity, built AI models to predict gRNA performance, and provided an online tool for high-fidelity genome editing. In molecular probe design, motivated by the progress of natural language processing (NLP), chemical molecules can be naturally viewed as a language to some extent (Weininger, 1988; Li and Jiang, 2021). Adapted to chemical language, NLP models like large language models (LLMs) enable tasks ranging from synthesis prediction to molecular generation in click chemistry. Li and Jiang (2021) developed molecular bidirectional encoder representations from transformers (Mol-BERT) to leverage deep contextual embeddings of molecular substructures, accelerating the AI-driven design and screening of clickable probes with tailored physicochemical and bio-orthogonal properties.

It is important to advance and apply AI in more complex chemical communications in the future. These models facilitate in-depth research into the chemical communication networks governing plant–microbe interactions, enable the monitoring and simulation of underlying molecular mechanisms, and guide the development and utilization of microbial, metabolic, and germplasm resources. Integrating these findings with smart agriculture systems enables precise interventions and enhances crop stress tolerance (Fig. 2d).

AI faces challenges in chemical communication. Although data heterogeneity in multi-omics data analysis has vastly improved, it still limits the generalizability of models (Zhao et al., 2023). AI applications in genome editing and click chemistry remain limited, with underdeveloped models for evaluating post-editing effects (Rees et al., 2021) and transboundary probe specificity (Chen MM et al., 2024). Microbial and chemical signal detection is affected by host genetics and environmental fluctuations (Zhan et al., 2022), highlighting the need for AI to monitor their real-time dynamics. Further integration of AI with chemical communication is essential for developing scalable and sustainable agricultural solutions (Fig. 2d).

4 Conclusions and outlook

Here, we systematically outlined the intricate chemical communication networks that govern plant–microbiome and intra-microbiome interactions. These networks enable plants to recruit beneficial microbes while selectively repelling pathogens (Zhan et al., 2022; Lv et al., 2023). Disrupting these networks may compromise plant fitness and increase susceptibility to environmental stresses (Leach et al., 2017). Beyond plant–microbiome and intra-microbiome interactions, these chemical networks extend into plant–plant communication and even the broader ecosystem (Midzi et al., 2022). Non-contact interactions enable rapid environmental responses, fostering ecosystem adaptability and resilience (Leach et al., 2017).

The application of the designed interdisciplinary technical framework can interpret chemical communication more comprehensively and efficiently, providing a more scientific solution to the existing research gaps in plant–microbiome and intra-microbiome interaction research. Multi-omics methods provide insights at the ecosystem level by integrating data. Multi-dimensional data analysis is performed using AI models to dig out key genes, proteins, and compounds related to chemical communication (Luo et al., 2022; Muller et al., 2024). Genome editing supports the verification of the function of key molecules at the genetic level. AI further advances this process by enabling the rational design of Cas proteins and gRNAs for specific genetic targets (Gao, 2021; Liu et al., 2023). Click chemistry allows real-time biomolecule tracking and pathway targeting, and its integration with AI supports specific probe design and interaction visualization (Chen MM et al., 2024). Finally, AI accelerates the translation of fundamental research into applications for smart agriculture (Zhan et al., 2022; Zhao et al., 2023).

Despite significant advancements in methodology, critical challenges persist in decoding chemical communication. The growth-defense trade-off remains a central paradox in plant immunity. Although recent studies have shown that the microbiome can alleviate this trade-off by optimizing plant metabolic allocation (Ku et al., 2024), the specific molecular mechanisms underlying this optimization remain unclear. Furthermore, the molecular mechanism underlying how environmental fluctuations affect chemical communication remains poorly understood. Integrating relevant environmental variables and in-depth research on chemical communication into experimental design is essential for building accurate predictive models and optimizing key parameters (Lotterhos, 2024). Future research should explore SynComs guided by chemical communication and engineered for optimal chemical signaling to enhance plant nutrient acquisition, stress tolerance, and disease resistance.

As crop diseases increasingly threaten global food security (Stukenbrock and Gurr, 2023; Pan et al., 2024), a deeper understanding of chemical communication within the plant–microbiome and intra-microbiome interactions is urgently needed. Technological advances will further strengthen the application of interdisciplinary approaches, empowering future research to harness their full potential in fostering resilient and sustainable agricultural systems.

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Author contributions

Mengcen WANG, Hongfu LI, and Xiaoyu LIU provided the original idea. Hongfu LI, Yaxin HU, Siqi CHEN, and Xiaoyu LIU wrote the manuscript. Hongfu LI, Yaxin HU, Siqi CHEN, Yusufjon GAFFOROV, Xiaoyu LIU, and Mengcen WANG revised the manuscript. All authors have read and approved the final manuscript.

Compliance with ethics guidelines

Hongfu LI, Yaxin HU, Siqi CHEN, Yusufjon GAFFOROV, Mengcen WANG, and Xiaoyu LIU declare that they have no conflicts of interest.

This review does not contain any studies with human or animal subjects performed by any of the authors.

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