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Review

Composing a microbial symphony: synthetic communities for promoting plant growth

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Plant microbiomes are pivotal for host development, influencing growth, health, fitness, and evolution, and have emerged as promising resources for sustainable agriculture. However, leveraging these microbiomes to improve crop yield and resilience is challenging due to the huge diversity of plant-associated and soil microorganisms and their intricate interactions. Recently, synthetic microbial communities (SynComs) have been exploited as a reductionist approach to harness microbial benefits and to understand multispecies interactions. Additionally, the advanced functionality of SynComs promises to surpass classic single-strain-based biosolutions. Nevertheless, challenges remain in designing customized, robust, and predictable SynComs for agronomic use. Here, we synthesize and discuss the logical and implemented approaches used to design and assemble SynComs, highlighting important principles, challenges, and trends in utilizing SynComs as alternatives to agrochemicals.

Highlights

SynComs, artificially assembled microbial communities, represent simplified, modular tools to investigate microbiome assembly and dynamics, as well as microbiome–host interactions, for promoting plant growth.

Current SynCom studies showcase adaptations of bottom-up and top-down approaches, including functional screening of strains and host selection to produce SynComs with a specific focus, such as phylogenetic member distribution or plant-related functionality.

Quantitatively synthesizing current research on SynComs for plant growth-promotion highlights common trends and challenges, as well as widespread discrepancies in the methodologies and principles applied to SynCom construction and evaluation.

Optimized SynCom construction should consider the concepts of stability, resilience, and reproducibility, and would benefit from the sharing of common building protocols.

Introduction

All plant tissues host diverse and functional microbial communities, known as the plant microbiota. Certain members of these communities, especially those living in the rhizosphere, are essential for plant development, health, and fitness in agroecosystems, coevolving with the plant as a holobiont [1–5]. These microorganisms are often referred to as the plant's second genome, extending the plant's genetic and metabolic capabilities [1,6]. Typically, in plant-associated microbiomes, bacteria and fungi are the most predominant and well-studied life forms. However, other groups such as archaea, viruses, nematodes, and protists contribute significantly to the overall plant benefit and microbiome assembly [7–9].

Now more than ever, harnessing the plant microbiota is being recognized as an essential approach for increasing the sustainability of food production, particularly as traditional agricultural practices face challenges amplified by climate change, soil degradation, and the demand to reduce chemical pesticide usage while maintaining profitable yields [10–12]. In response, research efforts have focused on identifying and testing individual microorganisms across various crops, offering a robust alternative for sustainable crop management. Consequently, a diverse array of strains demonstrating plant growth-promoting properties is utilized as inoculants to enhance plant yield and development [13,14]. Direct benefits to the plants include nutrient mobilization and transformation (e.g., nitrogen fixation), stress mitigation (e.g., drought tolerance), and protection from pathogens via competition, antibiosis, and enzyme production [13,15]. Alternatively, microorganisms can indirectly benefit the host by boosting intrinsic resistance mechanisms [16].

Although the use of microorganisms as inoculants for biocontrol and plant growth stimulation is becoming widespread, several key challenges must be addressed to fully capitalize on their potential to enhance crop productivity [12,17]. For instance, it is well known that the efficacy of a

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microbial inoculant (see Glossary), once released to the field, differs from the results obtained under *in vitro* and greenhouse assays, and varies with climate, soil type, and other environmental conditions [18,19]. Therefore, to harness the beneficial impact of microbial inoculants for plant health, it is urgent to develop new experimental approaches and conceptual frameworks that recognize microorganisms as entities living in complex assemblages, surrounded by interacting partners and modulated by the host [9].

In recent years, the use of **SynComs** has gained momentum to move beyond single-strain microbial inoculants (Box 1). This novel approach relies on the idea that selecting and assembling multiple species with complementary traits can lead to a modular, low-complexity consortium with unique community-level **emergent properties** that enhance the overall effectiveness. There is a growing body of evidence suggesting that such complex microbial consortia perform better than individual strains, can be engineered to fulfill a desired function, and are pivotal for studying various aspects of plant–microbiome interactions, including the underlying mechanisms that modulate the interactions among different community members [20,21]. Subsequently, the rational design and applied use of SynComs hold promise as an experimental and conceptual approach that might facilitate the translation of mechanistic and ecological knowledge of plant–microbiome interactions into innovative and sustainable crop-management plans.

In this review, we offer a comprehensive description of the current strategies for constructing, studying, and applying SynComs. In addition, we address bottlenecks, conceptual and experimental gaps, and discuss novel approaches in plant–microbe interaction studies to advance the rational design and use of SynComs for sustainable agriculture. To do so, we conducted an extensive search of studies published between 2002 and 2024 using Google Scholar, Web of Science, PubMed, and Scopus databases. The search primarily but not exclusively included the terms ‘synthetic community’, ‘plant’, ‘microbial mixtures’, or ‘microbial consortium’. Our searches yielded 86 relevant studies that met the following criteria: (i) microbiome members that were artificially assembled, (ii) SynComs comprised at least two members, (iii) the SynCom was either applied to plants or the members were isolated from plants; (iv) the SynComs fulfill specific functions, such as plant-growth promotion. Our literature synthesis compiles and analyzes up-to-date research in this field, aiming to unify and uphold the best practices for SynCom design and application, thereby facilitating their adoption in agricultural practices.

Construction of SynComs

The optimal design and characterization of SynComs are critical steps in harnessing microbial communities for agriculture applications. Building a tailored and function-enhanced SynCom for a specific crop is an all-around challenging task. It starts with the selection of representative members that mimic the taxonomic and functional traits of a plant-associated microbiome and extends to assess their effectiveness in field applications [21,22]. Typically, the principles guiding SynCom assembly are broadly classified either as **bottom-up** or **top-down** approaches. The bottom-up design selects and assembles individual microbial strains as building blocks based on their functional traits to achieve emergent properties unattainable through single-strain inoculation [23,24]. By contrast, the top-down approach starts with a complex natural microbial community, identifies the abundance or prevalence of taxa and assembles a subset of them aiming to recapitulate the diversity, specific composition, and functionality of a given microbiome [25–27].

The literature survey revealed that the bottom-up approach is commonly used for SynCom assembly. Out of 86 studies analyzed, 49 employed the bottom-up principles (Figure 1). A common trend in these studies is the isolation of SynCom members from the plant host to which they are intended to be applied, or the use of well-characterized strains from culture collections. During the

Glossary

Biofilm formation: a process by which microorganisms attach to a surface, grow, and produce extracellular matrix that facilitates adhesion, or form aggregates without surface attachment. Several plant-growth-promoting rhizobacteria form biofilms around the plant root to enhance root colonization and convey benefits to plants, such as nutrient uptake.

Bottom-up: a design approach that assembles SynComs from individual microbial strains with known and well-characterized traits, functionalities, and interactions.

Core microbiome: a set of taxa that consistently occur in a specific habitat or host with relatively high taxon abundance and occupancy. These taxa are hypothesized to be the most ecologically and functionally relevant microbes associated with that environment or host.

Emergent properties: characteristics or functions of a community that arise from interactions among different species, leading to new functions that exceed the sum of the individual contribution of each member.

High-throughput microbial culturomics: an advanced approach that employs diverse growth conditions, media, automation, and machine learning to cultivate, isolate, and identify a broad array of microorganisms from complex samples. This approach is less labor-intensive, and scalable, allowing for the integration of phenotype-genotype data, enabling the discovery and characterization of previously unculturable microorganisms.

Keystone taxa: taxa that play a unique and crucial role in microbial communities, highly interconnected with other taxa, and exert a considerable influence on community structure. The removal of keystone taxa can lead to a dramatic shift in community structure and function.

Microbial inoculant: agricultural amendments composed of beneficial microorganisms that act as biostimulants or biocontrol agents.

Network analysis: an exploratory data analysis approach that investigates co-occurrence patterns and associations among microbial taxa derived from metataxonomic or metagenomic data.

selection process, the compatibility of these members is tested to ensure that they can coexist, at least under *in vitro* conditions. The selected members often show a high frequency of **plant-growth-promoting traits** (**PGP traits**), which are measured *in vitro* as a proxy for *in planta* performance and functional contribution to the SynCom. For instance, Kaur *et al*. [28] assembled a four-member SynCom comprising *Arthrobacter*, *Enterobacter*, *Brevibacterium*, and *Plantibacter* species; these strains were selected based on complementary PGP traits, including indole acetic acid (IAA) production, phosphorus solubilization, and biocontrol activity against *Fusarium oxysporum*. Greenhouse experiments demonstrated that this SynCom enhanced the growth and fitness of cotton cultivars compared with single-strain inoculations [28]. Similarly, Yin *et al*. [29] evaluated ten distinct SynComs from a pool of 14 strains with PGP traits originally isolated from the wheat rhizosphere for suppressing root rot caused by *Rhizoctonia solani.* They described that certain combinations of strains were more effective to control the pathogen, highlighting the importance of synergistic interaction within SynComs [29].

By contrast, the remaining 37 studies focused more on top-down approaches. These SynComs aim to mirror the complexity and functionality of natural habitats, relying on the use of metataxonomics technologies (20/38 used next-generation sequencing methods) and experimental methods to manipulate the initial microbiome such as perturbations, community transplantation and host-mediated microbiome selection (Dataset S1 in the supplemental information online). For example, Li *et al*. [30] employed this framework to construct a simplified SynCom that conferred resistance to root rot disease. By profiling the root-associated microbial community of healthy and diseased plants, they identified and selected high-abundance bacteria and those enriched in diseased roots. The simplified SynCom demonstrated synergistic protective effects on plants by inhibiting fungal pathogen growth and activating plant-induced systematic resistance [30].

Both bottom-up and top-down approaches have been instrumental for building functional SynComs, yet each approach presents specific conceptual and operative bottlenecks. The bottom-up approach, despite its widespread use and the precise selection of members with specific traits, could oversimplify higher-order microbial interactions given the reduced member

Niche complementarity and selection effects: complementarity occurs if species differ in resource utilization and facilitate each other, whereas selection occurs if interspecific interactions lead to the dominance of species with higher productivity in mixed communities.

Plant-growth-promoting traits (PGP traits): characteristics or functions of certain microorganisms that facilitate plant growth or health. These traits include nutrient mobilization (e.g., phosphorus or nitrogen fixation), production of phytohormones (e.g., auxins, cytokines), antagonistic activity against pathogens, induction of systemic resistance, and alleviation of stress tolerance.

SynComs: artificially assembled microbial communities composed of a defined population of microbial species.

Top-down: a strategy for building SynComs by selectively simplifying complex natural microbial communities to replicate the diversity and functionality of a targeted microbiome.

Box 1. Historical development and conceptual evolution of SynComs

The field of plant rhizosphere microbiology emerged in the late 19th century [90]. Influential works on the proliferation of soil bacteria colonizing root surfaces, the discovery of nitrogen fixation by legume-nodulating bacteria, and the rhizosphere-mediated influence on plant growth and development marked the beginning of a series of significant discoveries [91]. These findings have since substantiated the widely accepted notion that microorganisms are indispensable components of plant health which led to the establishment of a discipline on plant–soil–microbe interactions. Since its foundation, this discipline has been driven by the idea of isolating axenic cultures, perhaps also motivated by Koch's postulates that aim to establish a causal relationship between a microorganism and a disease. Subsequently, under the 'single-strain' paradigm, several studies have reported how specific strains impact plant development in addition to the underlying mechanisms. This prolific period solidified the concept that strains of rhizosphere bacteria stimulate plant growth, leading to the formalization of the conceptual framework of plant-growth-promoting rhizobacteria by Kloepper and Schroth in 1980 [92].

From a single strain to a symphony of microbes, scientists began to consider whether introducing a diverse microbiome community could amplify the benefits of plant growth promotion. This includes the transfer of microbiomes from a rhizosphere soil of a healthy plant into a conducive environment [93–95]. This approach, like fecal microbiome transplants in human gut health research, aims to establish beneficial microbial communities by directly transferring the microbiome from a healthy donor to a susceptible recipient, potentially controlling diseases caused by soil-borne pathogens [96,97]. In the same conceptual framework, another approach involves the development of plant-associated microbial communities through artificial selection mediated by the host. Here, entire communities are passed across multiple generations by selecting replicates with enhanced plant traits [64,90–92] (Figure I).

Among the various approaches, the development of a multistrain consortium, or SynCom, is by far the most widely studied and used approach in the plant–microbe–soil interaction field. In microbiome research, a synthetic community is an artificially assembled microbial community built by mixing selected strains [83,98]. The published research on SynComs has grown significantly since 2014 [99]. SynComs were first applied to study complex interactions in synthetic biology and the gut microbiota field. Inspired by these, SynComs aim to mimic natural soil microbial communities or select representative plant-associated microbiomes and designed consortia with complementary beneficial traits. This strategy can potentially lead to more consistent and robust effects in field applications [54,99,100]. In addition, given their low complexity and high modularity, SynComs are gaining attention as a tool to explore the ecological and genetic mechanisms underlying microbiome assembly, successional dynamics, and resilience, as well as establishing causal relationships between microbiome composition/activity and host phenotypes.

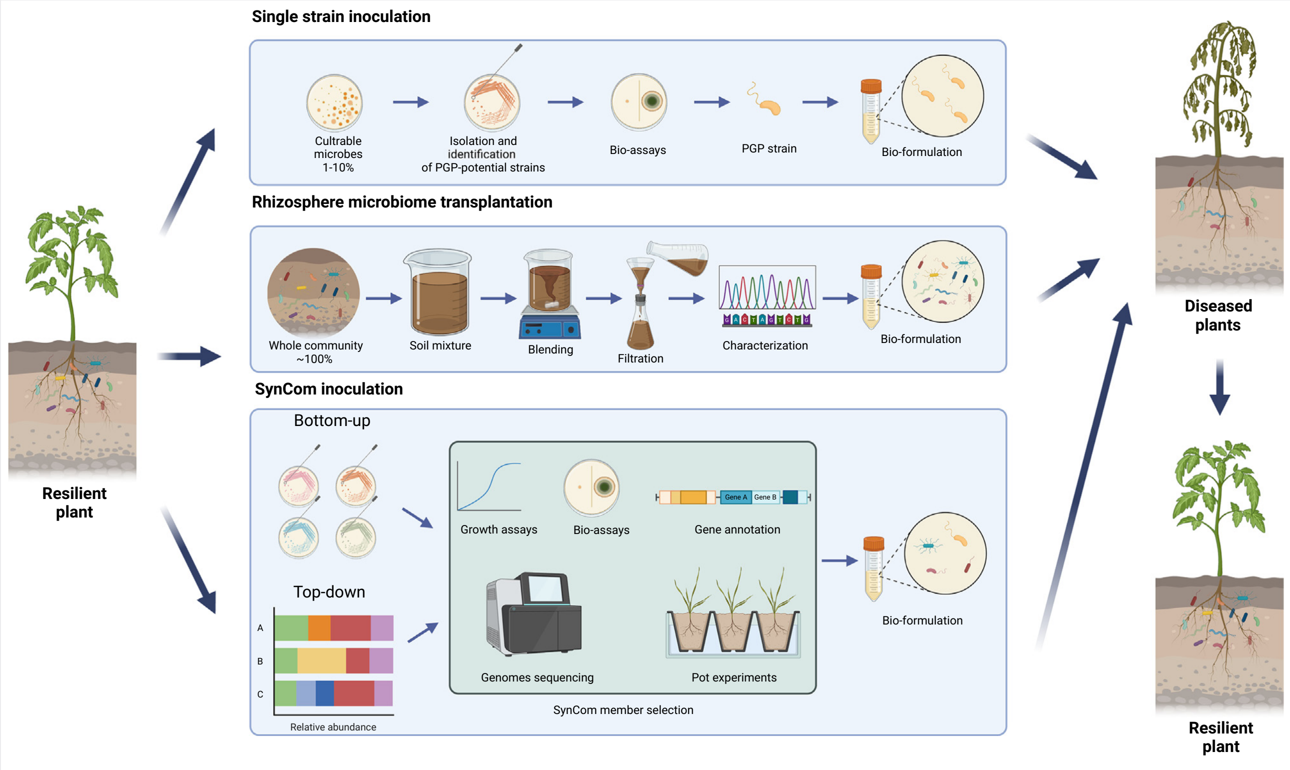

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Figure I. Historical development of beneficial plant-associated microorganism applications. The agricultural use of beneficial microorganisms began with single-strain inoculation, which involves isolation, identification, characterization, and application of a single microbial strain to plants. More recent advancements include rhizosphere microbiome transplantation, a culture-independent method that transfers the entire microbial community from a donor plant to a recipient plant. Another innovative approach is SynCom inoculation, where community members are selected using either bottom-up or top-down strategies. These members undergo growth assays, genome sequencing, gene annotation, and pot experiments to develop a defined microbial community that serves as a bio-formulation for inoculating diseased plants. The figure was created with BioRender.com. Abbreviation: PGP, plant-growth-promoting traits.

composition. This can lead to a suboptimal performance in natural conditions, where diversity and emergent properties can be critical. Additionally, constructing bottom-up SynComs is labor-intensive, requiring extensive screening and selection to identify strains with relevant traits and compatibility with other community members, whereas top-down approaches naturally tend to select resident microbes that have high compatibility with the plant and its microbiome (Figure 2).

Conversely, SynComs assembled using top-down approaches face issues related to predictability, control, and applied uses. These communities mimic better the microbiome composition but may be more difficult to manipulate, maintain, and direct toward desired functions if a larger number of SynCom members are utilized [31]. Moreover, top-down approaches rely on sequencing technologies and often assume that the presence of a specific genomic signature or prevalent taxon directly translates to functional activity, as evident by their use of **core microbiome** analysis for SynCom member selection (Figure 2).

These drawbacks highlight the need for more advanced selection and testing protocols to improve the use and effectiveness of SynComs for sustainable agriculture. Over the past decade, various SynCom design principles combining elements of both approaches with computational

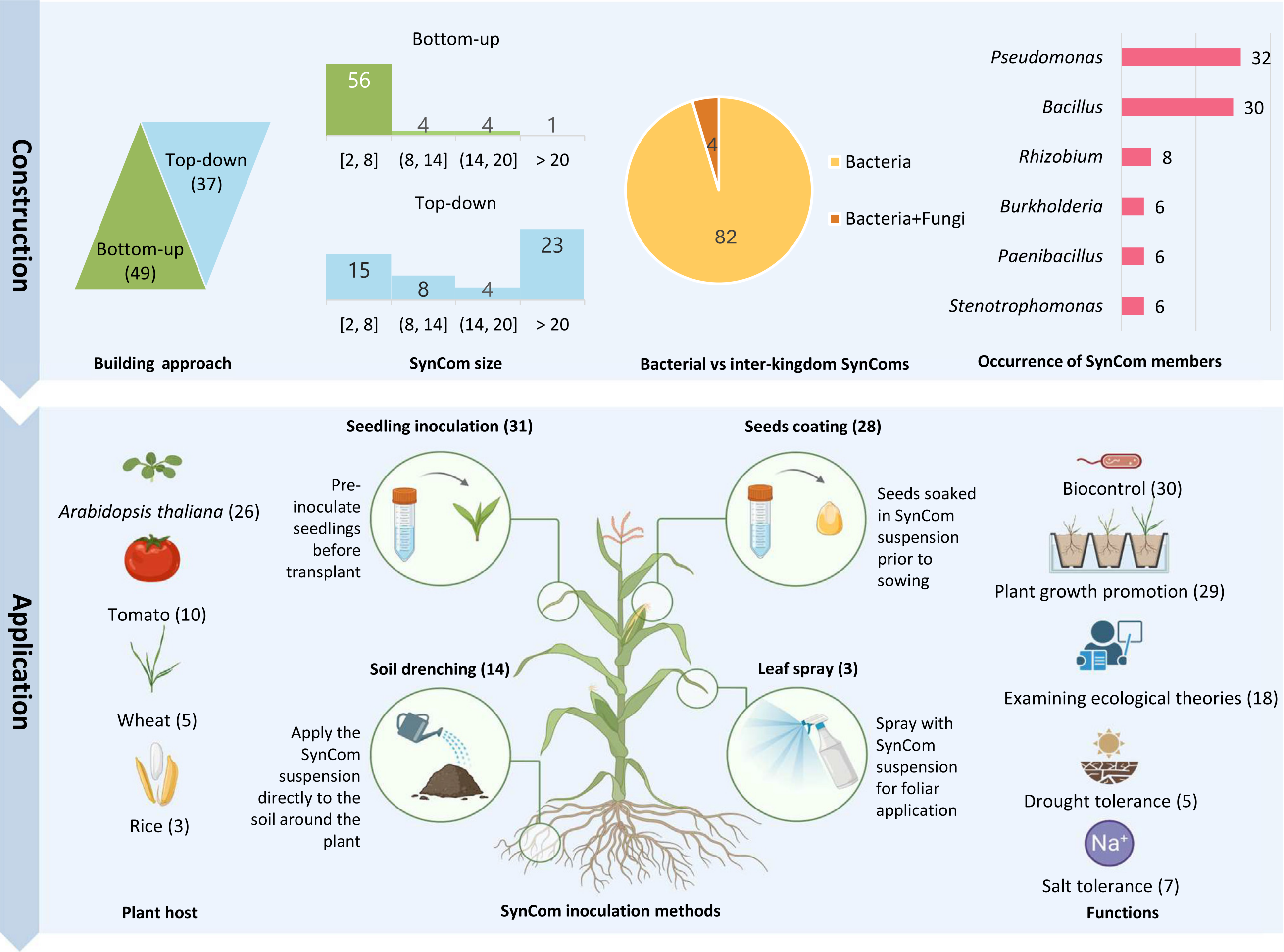

Figure 1. Overview of SynCom (synthetic microbial community) construction approaches and applications derived from 86 studies. The figure highlights the number of SynCom construction approaches, the distribution of SynCom sizes, the proportion of bacteria-only versus interkingdom SynComs, and the occurrence frequency of SynCom members. Additionally, the applications of SynComs in various plant species, inoculation methods, and functional roles are highlighted. The numbers in each panel represent the number of studies exhibiting the respective feature.

approaches (Box 2), have been explored for diverse applications. One common method is taxonomy or phylogeny-based SynCom assembly that involves exploring microbiome composition across diverse or contrasting samples to identify a core microbiome or the most prevalent taxa that might include the potential target taxa/strains, which are then iteratively selected to form minimal SynComs [32–37]. Bai *et al*. provide an example for this approach by identifying a bacterial core microbiome across the leaf, root, and rhizosphere soil of *Arabidopsis thaliana* (arabidopsis). The authors constructed SynCom from these core strains and tested them on germ-free arabidopsis plants to study microbiome functionality and niche adaptation [38]. Likewise, Carlström *et al*. utilized a larger, diverse set of bacterial isolates, distinguishing strains by 16S rRNA sequencing, and studied SynCom establishment in the arabidopsis phyllosphere, further dividing strains by phylum to analyze drop-out and late-introduction effects [39]. An alternative approach focuses on selecting and assembling members purely in functional and phenotypic traits either at the individual-strain or community level [24,40–42]. The enhancement of phenotype and trait varieties has been the goal of these designs. Examples include alleviation of drought and

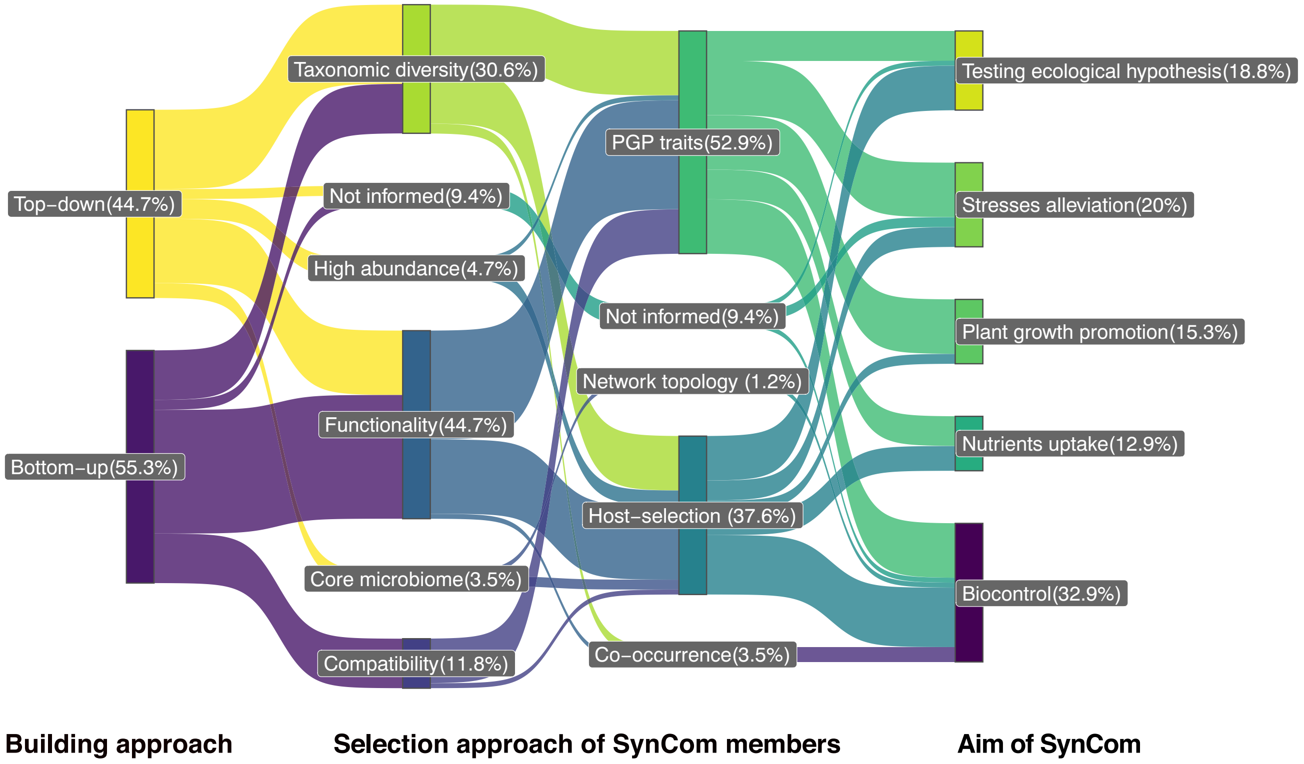

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Figure 2. Summary of meta-analysis on current SynCom (synthetic microbial community) construction approaches. The first classification on the left is based on whether a top-down or bottom-up workflow is applied, followed by the primary rationale for choosing the SynCom members, with the most prominent being 'Functionality' and 'Taxonomic diversity'. Subsequent parameters informing member selection mostly involve testing the microorganisms' Plant-growth-promoting traits (PGP) or performing host-selection experiments. These selection methods have been ingeniously combined to create SynComs for a variety of goals (right column).

salt stresses [24,43–52], plant-growth promotion [33,34,53], **biofilm formation** and root colonization [24,52,54,55], and control of pathogens [27,29,56,57]. In addition to these principles, from 2015 onwards novel SynComs have been increasingly established through the so-called host-mediated selection approach (20/86). This approach relies on the ability of the host to selectively enrich microbes that confer beneficial traits through iterative cycles of growth [58,59]. For example, Niu *et al*. [26] used host-mediated selection to develop a simplified SynCom for maize roots with seven key strains. This community stably colonized maize roots, mimicked the natural microbiome composition, and inhibited *Fusarium verticillioides*. In this SynCom, *Enterobacter cloacae* has been identified as a keystone species crucial for community structure and function [26].

The aforementioned approaches have significantly advanced SynCom development and application. However, a central question, with both conceptual and practical implication, remains open: what is the optimal size and taxonomical composition for a SynCom to be effective in agricultural applications? Among the 86 studies reviewed, most of them highlight the need for balancing community size and composition in order to reduce complexity, mimic at some extent the natural composition and functionality, while keeping the modularity and ease the *in planta* applicability. In terms of SynCom sizes, the member composition ranges from two to 30. SynComs assembled through a bottom-up approach typically have a median size of four members. By contrast, SynComs assembled through a top-down approach have a median size of 16 members, ranging from two to 218. The impact of SynCom size on functionality is a complex and open debate

Box 2. Advancing mechanistic insights into SynComs: leveraging omics, modeling, and network analysis

Once a SynCom is established, mechanistic understanding of the interactions among SynCom members and identification of emerging functional properties are crucial for optimizing SynCom performance (e.g., plant growth promotion) in addition to addressing challenges related to SynCom stability, scalability, reproducibility, and resilience to environmental perturbations.

Mechanistic understanding of SynCom dynamics can be acquired from various omics approaches concentrating on taxonomic diversity, transcriptome, proteome, or metabolome. Metataxonomics have been particularly useful in evaluating the stability or persistence of SynCom members and monitoring their development over time. This approach offers enhanced efficiency and accuracy compared with traditional plating for estimating the member abundance and dynamics. For instance, Schmitz *et al.* employed 16S rRNA amplicon sequencing and co-occurrence **network analysis** to estimate the relative abundance of each member of a SynCom that was designed to alleviate salt stress in tomato plants [47]. Nevertheless, metataxonomics has its limitations, as the presence of multiple 16S rRNA operon copies and limited sequence variation among closely related taxa hinder the accuracy of species identification [101]. These limitations restrict strain-level taxonomic resolution and miss functional aspects of SynComs [102]. Therefore, metagenomic analyses are used to gain detailed insights into microbial functionality and, for instance, identify key genes within the root microbiota of healthy plants [103].

Computational models can assist in predicting emergent properties resulting from complex interactions among SynCom members. Due to the nonlinear nature of emergent properties, they cannot simply be inferred by summing the properties of individual SynCom members. Thus, computational models are imperative for establishing casualties between community composition and function [104]. The use of genome-scale metabolic models (GEMs/GSMM) is one of the approaches for modeling emergent properties and community dynamics [105]. These models, constructed from genomic assemblies, simulate the metabolic phenotypes of microorganisms and their responses to environmental and genetic perturbations [106]. By translating the biochemical reactions encoded in genomes, GEMs enable the selection of a minimal community encompassing essential compounds for microbial metabolism and genes associated with PGP traits [107–109]. Although such constructed SynComs have yet to be validated in plant experiments, these studies expand our toolkits and represent an innovative *in silico* approach for SynCom construction and understanding.

When comparing the developments within the gut and plant microbiome fields, gut microbiota SynCom establishment is grounded on various pillars lacking in the plant SynCom field. For instance, the gut microbiota field benefits from a wealth of genomic data at the genus and species level, including well-characterized functions and metabolic profiles. Additionally, constantly updated databases and bioinformatic tools are readily available for gut microbiome analysis. By contrast, the plant SynCom field faces multiple challenges due to the so called ‘dark matter’, the uncultured plant-associated microbiome, unannotated genes and proteins, and unknown metabolic pathways. These unknowns hinder the construction and calibration of mathematical models, as they rely on available experimental data.

Network analysis expands the comprehension of ecological interactions within SynComs and enables the identification of highly interactive members within the networks, termed ‘keystone’ taxa which play crucial roles in suppressing the growth of pathogens or promoting the expression of plant-beneficial genes [92,110]. Additionally, characterizing network topologies enhances evaluation of SynCom dynamics, for example, integrating plant host phenotype with microbiome networks facilitates SynCom design [111]. Together with machine learning, network analysis can assist in inferring associations between plant phenotype and microbiome, thereby elucidating causality among taxa and host outputs, such as plant yield or disease. Nevertheless, we recommend caution in interpreting these networks, as both experimentation and mathematics have shown that interactions suggested by network analysis may not be accurate. Conducting *ad hoc* experiments and incorporating biological information into network analyses could potentially help to create robust mechanistic interpretations.

[60–62]. Increasing the number of strains can enhance functional diversity, resource usage, and plant benefits through mechanisms like **niche complementarity and selection effects** [63–65]. However, in some cases, the relationship between diversity and functionality may have unintended drawbacks. For instance, many bacteria are functionally redundant, meaning that adding more species does not necessarily enhance ecosystem functioning. Moreover, higher diversity can lead to a high frequency of antagonistic interactions among members, negatively influencing community performance and stability [66].

Regardless of the chosen assembly approach, SynComs are primarily assembled using bacterial species (Dataset S1). Listing and counting the genus composition of bottom-up assembled SynComs suggest that the taxonomical composition of these SynComs is biased towards readily cultivable strains with PGP traits, including *Pseudomonas* (32 occurrences), *Bacillus* (30), *Rhizobium* (eight), *Burkholderia* (six), *Paenibacillus* (six), and *Stenotrophomonas* (six). Assembling a purely bacterial SynCom may simplify design and scaling-up cultivation requirements, but it could potentially limit the overall performance, since low-abundance taxa and other organisms like fungi or protist have been suggested to be key players in microbiome functioning [32,67]. Evidently, the design and evaluation of cross-kingdom SynComs are in their infancy due to the operational challenges with including high-order organisms. Incorporating fungi or protists would require additional considerations regarding nutrient sources, growth conditions, and extended knowledge of inter-kingdom interactions [68]. However, Zhou *et al*. demonstrated the feasibility of combining fungal and bacteria strains in a SynCom to protect tomato plants against Fusarium wilt disease [56]. Additionally, mutual selective pressures on plant hosts and their associated microbial communities have been hypothesized to drive the evolution of beneficial inter-kingdom microbe–microbe interactions, favoring these complex interactions rather than associations with a single microbial class [32,68].

Aims and uses of SynComs

From an agronomical perspective, application of SynComs is aimed at enhancing overall crop growth, performance, and resilience under relevant cultivation conditions. Accordingly, SynComs have been evaluated for their ability to confer fitness advantages on plants, including stress tolerance, nutrient uptake, growth promotion, and resistance to phytopathogens. Abiotic stress – such as drought, salinity, and temperature fluctuations – poses a major threat to agricultural productivity [69]. Plant-associated microbial strains can mitigate these stresses via mechanisms including osmoprotectant synthesis, modulation of hormonal pathways, or improving antioxidant activity on plants [70]. Consequently, several SynComs have been developed to alleviate stress. For instance, a five-member SynCom assembled using strains isolated from the desert plant *Indigofera argentea* increased the biomass of salt-stress tomato plants by activating salt-stress-related genes and stimulating ion accumulation [47]. Similarly, Yang *et al.* demonstrated that a four-member SynCom improved drought tolerance of *A. thaliana* by increasing chlorophyll and abscisic acid levels. Notably, drought tolerance induction was a community-level property, as the biofilm-forming SynCom had a greater influence than the individual strains [24].

In addition to coping with abiotic stresses, counteracting plant diseases is essential for sustainable food security. Microbiomes and SynComs offer tailored, eco-friendly alternatives to the overuse of agrochemicals since they can protect plants from pathogens through secretion of antimicrobial metabolites, cell-wall-degrading enzymes, and induction of plant systemic resistance [16,71]. The study by Li *et al.* demonstrated that the added SynCom protected *Astragalus* plants from Fusarium infection through direct pathogen inhibition by producing antimicrobial metabolites and through indirect enhancement of the plant systemic defense [30]. Similarly, Prigigallo *et al.* showed that the tested SynCom reduced Fusarium wilt in banana plants through suppression of pathogen growth by volatile organic compounds and through a fungal cell-wall-degrading enzymatic activity [72]. These examples, along with those depicted in Dataset S1, underscore the potential of SynComs to be integrated in crop management plans facilitating the transition toward sustainable agriculture.

SynComs as models to test ecological hypotheses in plant–microorganism interactions

SynComs, beyond their role as plant biostimulants, can be used to elucidate fundamental molecular, ecological, and evolutionary mechanisms underlying plant–microorganism interactions. As simplified and well characterized systems, SynComs can serve as valuable models, or even be a prerequisite, for understanding complex interactions in natural systems [73,74]. From the 86 publications, 19 studies explored general ecological or evolutionary processes. A recurring theme in these studies is the connection between host genotype and phenotype, as well as the composition and functionality of the microbial community. For instance, the role of plant specialized metabolites has been tested for dictating bacterial composition of an *A. thaliana* root-derived SynCom. Coumarins caused a shift in microbial composition by specifically inhibiting *Pseudomonas* strains via a redox-mediated mechanism [75]. Similarly, Bodenhausen *et al.* used a SynCom representing the most abundant phyla in the arabidopsis phyllosphere to unveil host genetic factors affecting community abundance and composition; from a panel of 55 plant mutants, they found that alleles associated with cuticle synthesis and ethylene signaling influence SynCom community structure [76]. SynComs have also been exploited to evaluate the contribution of richness and composition to the bacterial ecosystem services. In these approaches, experimental frameworks include multiple combinations of the microbial species from monocultures to highly diverse communities to identify the high-performance consortia that exert benefit to a plant [63,77,78]. Using this approach, Rhadi *et al.* tested the impact of a species-richness gradient (0, 1, 3, 5, or 6 species per community) on plant growth, nutrient assimilation, and soil nutrient dynamics via seed-inoculation. They found that the plant biomass increased as a function of SynCom richness but not nutrient assimilation [79]. Analogously, Wei *et al.* demonstrated that invasion success of the plant-pathogenic *Ralstonia solanacearum* decreased with species diversity and resource use network [62]. In addition, other ecological hypotheses such as priority effects [39,80], **keystone taxa** [39,52], host preference and recruitment [37], and the impact of initial microbiome composition in future plant health have been evaluated using SynComs [81]. Despite the current limited number of studies addressing broad ecological and evolutionary questions, these findings highlight the potential of SynComs to elucidate causal relationships between microbial composition and host phenotypes. Moving forward, expanding the number of SynComs and hypothesis to be tested will be essential to close the gap between simplified models and natural ecosystems but also to better inform the design and use of SynCom in agriculture.

Challenges and research gaps

The use of SynComs has been proposed as a promising tool to harness the potential of plant-associated and soil microbes in enhancing plant productivity under global climate change. However, like traditional single-strain inoculants, SynComs face challenges related to the efficient delivery of microorganisms into the soil, overcoming abiotic stressors, and ensuring robust colonization of plant compartments to express desired traits. Additionally, navigating complex regulatory frameworks adds further limitations to the commercial viability of SynCom-based inoculants [82]. Beyond these shared challenges, SynComs face unique, intrinsic hurdles that must be addressed for successful application in agriculture.

Designing and assembling a SynCom poses considerable challenges, beginning with the choice of the number and type of compatible community members. By design, SynComs must balance simplicity for practical application and diversity to retain ecological functionality that impact plant development. High-diversity SynComs, which are less frequent in the surveyed studies (Figure 1), could be impractical for field applications and industrial scalability due to the challenges in simultaneously handling and maintaining numerous strains [83,84]. However, overly simplified SynComs risk losing key ecological functions such as stability, resistance to pathogen invasion, and niche occupation as consequences of reducing diversity and excluding potential keystone species [24,36,84,85]. Thus, balancing diversity and functionality remains a bottleneck in building SynComs that exert a benefit as healthy plant-associated microbiota. These efforts are further limited by the low number of successful cross-kingdom assemblages and the exclusion of nonculturable microorganisms, particularly when SynComs are assembled via the bottom-up approach. Potential solutions to these limitations include the development of a robust conceptual framework that integrates microbial diversity, microbiome function, and plant health. Such a framework could encompass guidelines for selecting and prioritizing keystone species, and methods for assessing ecological interactions among SynCom members and their direct effect on plant development. On an operative level, advancements in the ability to efficiently select and screen the pool of potential and highly functional members of the SynComs are required. To do so, the use of **high-throughput microbial culturomics** approaches combined with computational approaches have gained traction in the recent years and offer promising solutions [86,87]. Additionally, synthetic biology tools can be adapted to engineer specific functions in the SynCom members for desired applications. Similarly, omics approaches can be used to identify key functional groups and keystone species, even if the microbes themselves are not culturable in pure cultures (Figure 3).

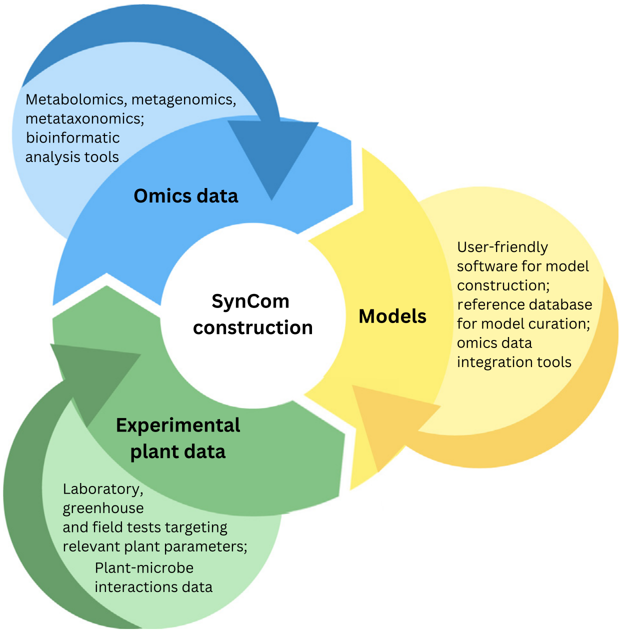

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Figure 3. Integrative approach for optimal SynCom (synthetic microbial community) construction. Optimal SynCom construction is the product of an iterative flow of information between experimental data, omics data, and predictive models. Each component relies on advanced, state-of-the-art technology and scientific knowledge to produce useful data. Both experimental data and omics data feed the construction of models, which in turn can inform further experiments.

Another potential challenge in the use and application of SynComs emerges from member dosification (the initial microbial concentration of each member in a SynCom) and the inoculation volume used in greenhouse and field trials. For single-strain inoculants, for instance, the efficacy likely depends on the initially applied concentration, the inoculation timing, and frequency [88]. Therefore, we might expect that the efficacy of SynComs depends on the same factors as single-strain application, but also additional parameters caused by the complexity of SynCom-based inoculants. However, our literature survey suggests that most SynComs are assembled using equal ratios of each member, which may ease the assembly of multispecies inocula for proof-of-concept experiments, but is likely unrealistic, as an equal initial ratio does not reflect the natural abundance of the SynCom members in a microbiome. Furthermore, a detailed exploration of the implications of specific growth medium requirements, different starting ratios and diverse growth rates of each SynCom member is still lacking or contradictory. Despite the importance of these factors, most studies neither vary the members inoculation and proportion nor evaluate the stability (or how composition changes over time) of the SynCom after inoculation (Box 3). Understanding these dynamics is crucial for optimizing SynCom design and deployment, and to predict the long-term performance of SynCom-based inoculants. Additionally, each strain's cultivation and formulation must be optimized for scalability, which increases the complexity and cost of industrial SynCom production. Moreover, optimized

Box 3. Stability, resilience, scalability, and reproducibility of SynComs

Stability is often associated with the establishment/survival of the SynCom members in a defined timeline. However, it can also be argued that stability in specific studies or applications goes beyond counting SynCom members, and instead, the retention of a function is more relevant. Whether stability should be a criterion for a SynCom is still debated, as many studies do not evaluate this aspect. The resilience of microbiomes, including SynComs, depends on the capacity of the microbiome to recover from perturbations, which is strongly linked to microbial diversity. Both scalability and reproducibility are important factors when designing SynComs for agricultural use, because without a robust and repeatable utilization of SynComs in larger scales such as greenhouses or fields, their value for agricultural applications decreases. Reproducibility between laboratories requires the SynCom to be stable and resilient to subtle changes in terms of temperature, humidity etc. This offers the opportunity to study a SynCom in different experimental setups providing additional knowledge about its functions and emergent properties.

downstream processes and in-field applications are equally essential to unlock the full potential of industrially produced SynComs.

In field applications, SynCom must follow regulations for bio-based products. In the EU, the use of microorganisms must meet safety criteria for humans, animals, and the environment. Furthermore, metabolites and their derivatives arising from the breakdown or transformation by SynCom members should equally be safe and need to be quantitatively tested *in situ* [89]. This presents a substantial challenge due to the 'black box'-like nature of plant-associated microbial systems, their interactions and by-products, where complexity increases with a higher number of SynCom members. Furthermore, SynCom stability within a resident microbiome is also considered during the approval process of a SynCom for agricultural use. A successfully established SynCom may permanently alter the microbiome, while the lack of SynCom establishment may offer a temporally limited effect with subsequent vanishing that avoids permanent environmental changes. It remains unclear whether the potential of long-term soil microbiome shifts is considered during the approval process. A closer consideration of legal requirements should be included during SynCom design processes as this may accelerate market approval.

Concluding remarks

Microbial diversity within a SynCom is influenced by the construction approach. The common goal behind development of the SynCom is to improve the future of agriculture, either through direct plant promotion or via creating a novel understanding of plant-associated community dynamics. However, several SynComs in the literature have not been evaluated on plants or have been tested on laboratory model plants, like *A. thaliana*. Our literature survey (Dataset S1) reveals a high discrepancy between the methods and approaches used for establishing and testing SynComs. We advocate for the development of standardized, shared methodologies regarding inoculation ratios, timing, and application techniques across different plant species (see Outstanding questions). Furthermore, we recommend testing SynCom stability over time to ensure the long-term activity of SynCom applications. Notably, SynCom stability has been assessed in only 35 of the 86 publications, all of which lack evaluation of SynCom performance and presence in later stages of application, including formulation and field experiments. The lack of common principles, protocols, and parameters while building a SynCom increases the difficulty to adequately compare the used approaches. Implementing shared protocols and incorporating expertise across laboratories should improve reproducibility and experimental efficiency. Yet, several challenges remain for SynCom construction, including the difficulty of handling larger SynComs, which may mimic the natural microbiome's complexity to a higher extent, but which suffer from lower reproducibility. Developing and implementing more advanced computational methods and larger scale screening of strains and communities can bring us closer to overcoming these hurdles and advance the already promising foundation of current SynCom developments.

Implementing SynComs in agriculture in combination or place of current approaches has the potential to positively impact our agricultural practices by manipulating the existing crop microbiomes to increase yield and provide protection from pathogens, decreasing the need for synthetic pesticides and fertilizers, benefitting not only crop yields but working towards improving the biodiversity of the surrounding fields.

Outstanding questions

What is the optimal size of SynComs that balance functionality, scalability, and reproducibility?

What are the optimal strategies for calibrating the ratio and inoculant volume of a SynCom, and at what developmental stage of the plant (i.e., seeds, juvenile plants, or mature form) should SynComs be applied to maximize their efficacy?

How can we better incorporate nonculturable microorganisms, and others whose establishment depends on interactions with other microbes into SynComs?

How should the scientific community work towards developing an efficient, unified, and streamlined approach for the construction and validation of SynComs?

How can we anticipate and address key principles in SynCom construction to streamline regulatory approval and accelerate SynCom application on the field?

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Declaration of interests

No interests are declared.

Supplemental information

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