



# Emerging strategies for precision microbiome management in diverse agroecosystems

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**Substantial efforts to characterize the structural and functional diversity of soil, plant and insect-associated microbial communities have illuminated the complex interacting domains of crop-associated microbiomes that contribute to agroecosystem health. As a result, plant-associated microorganisms have emerged as an untapped resource for combating challenges to agricultural sustainability. However, despite growing interest in maximizing microbial functions for crop production, resource efficiency and stress resistance, research has struggled to harness the beneficial properties of agricultural microbiomes to improve crop performance. Here, we introduce the historical arc of agricultural microbiome research, highlighting current progress and emerging strategies for intentional microbiome manipulation to enhance crop performance and sustainability. We synthesize current practices and limitations to managing agricultural microbiomes and identify key knowledge gaps in our understanding of microbe-assisted crop production. Finally, we propose research priorities that embrace a holistic view of crop microbiomes for achieving precision microbiome management that is tailored, predictive and integrative in diverse agricultural systems.**

Microorganisms are indisputably important for ecosystem health. From the wealth of research on microbial communities (that is, microbiomes) associated with soil, plants and animals, a spectrum of microbe-driven impacts on ecosystem function has emerged<sup>1–3</sup>. Microorganisms not only form specialized relationships with their hosts, but are also responsible for driving global patterns in carbon and nitrogen cycling<sup>2,4</sup>. For example, extreme dependence on microorganisms for nutritional requirements has repeatedly evolved in plants and animals<sup>5,6</sup>, enabling host organisms to live in habitats they would otherwise be excluded from. Microorganisms constitute more than 15% of the Earth's biomass<sup>7</sup> and are responsible for driving many ecological processes, including biogeochemical cycles and nutrient acquisition by plants<sup>2,4,8–10</sup>. It is therefore widely recognized that microorganisms are interwoven into the many layers of natural and managed ecosystem functioning.

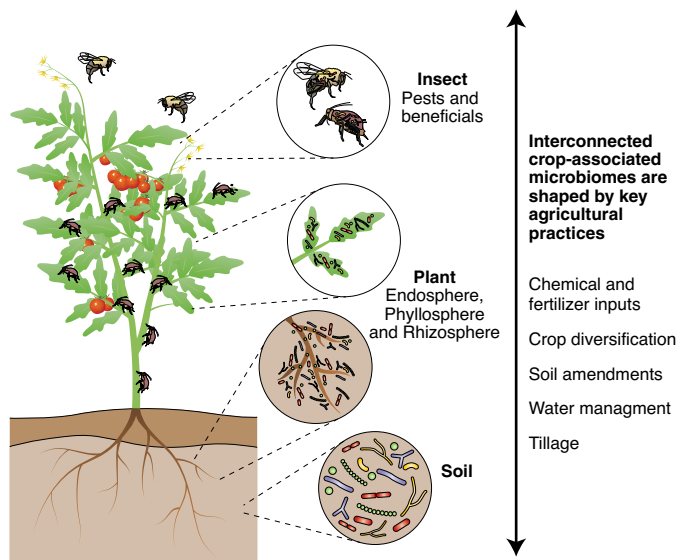
For decades, researchers have made considerable efforts to characterize the microbial communities critical for ecosystem health. Exponential growth in microbiome research has led to publication of several extensive reviews detailing the complex communities and many roles of microorganisms associated with soil, plants and insects (for example, refs. <sup>8,11–13</sup>). However, the current wave of interest in understanding how microbiomes impact the ecosystem has involved a substantial shift away from primarily cataloguing microbial diversity in different environments. Research efforts now aim to uncover the forces shaping microbiome structure and function, measure heritability of microbiome-derived host phenotypes and determine what processes govern microbiome stability and resilience to disturbance<sup>14–16</sup>.

Agroecosystems—ecosystems involving interactions between cultivated fields and surrounding natural areas—have become a hotspot for research focused on harnessing the beneficial properties of microbiomes for improved crop health and protection from stress<sup>15–18</sup>. Throughout the history of agriculture, humans have employed planting strategies that avoid build-up of soil-borne pathogens and intentionally used microorganisms to fight agricultural pests<sup>14</sup>. Yet, microbial communities associated with soil, plants

and insects are traditionally studied as distinct sectors, with limited cross-talk between disciplines. Recent research highlights the interconnected nature of microbiomes, particularly those associated with plants, soil, insect herbivores and pollinators<sup>3,17,19–21</sup> (Fig. 1). As appreciation for the complexity and interconnected nature of crop-associated microbiota grows, there is a clear need to unify our understanding of the processes driving microbiome assembly and function. Integrating knowledge across the overlapping sectors of crop microbiomes (that is, soil, plants and insects) has important implications for agroecosystem health and long-term sustainability, including establishing best management practices and advancing microbiome-based technology.

The current boom in microbiome research has reinvigorated interest in developing novel microbial biotechnology, but aside from a few successful cases (noted below) we have yet to capitalize on microbiome-centred approaches for improving crop health and agroecosystem sustainability. High-throughput sequencing and phenotyping capabilities now enable investigation of entire microbial communities and simultaneous screening of thousands of microorganisms for beneficial properties, which has spurred rapid growth of the microbial biotechnology sector<sup>22</sup>. The market value of biostimulants and biocontrol agents is projected to reach over US\$14 billion by 2023 (<http://go.nature.com/2MyMdmh>), but some products have garnered a 'snake oil' reputation, highlighting a need for improved testing and transparency in product development. In addition, we still lack guidelines for intentionally managing the interacting domains of agricultural microbiomes to improve crop performance and protection from stress. Numerous recent reviews suggest approaches for managing agricultural microbiomes (for example, refs. <sup>15,23</sup>), but without a comprehensive understanding of how traditional practices drive changes in all domains of crop-associated microbial communities (Fig. 1), progress will be slow. Crop protection problems in different agricultural systems will also require unique solutions, yet it is currently unclear how management of agricultural microbiomes should be tailored to meet a spectrum of needs.

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**Fig. 1 | The major sectors of crop-associated microbial communities (soil, plant and insect) are shaped by key agricultural practices.** Arrows highlight how soil, plant and insect microbiomes interact to influence crop health, and show how each is affected by the listed management practices. See Table 1 for summary and descriptions of management practices.

This Review brings together knowledge of current practices and limitations in managing soil-, plant- and insect-associated microbiomes (the phytobiome<sup>1</sup>) and outlines next steps for advancing microbiome-informed management across diverse agricultural systems. We synthesize the unintentional and intentional strategies used for microbiome manipulation and organize historical progress into ‘generations’ of agricultural microbiome research that reflect milestones in knowledge, approaches and technology. Finally, we conclude with discussion of fundamental knowledge gaps and emerging strategies for the future of precision microbiome management that are tailored, predictive and integrative.

### Impacts of management practices on agricultural microbiomes

Understanding the unintentional consequences of agricultural practices on crop microbiomes has important implications for steering microbial communities to produce intended beneficial effects and identifying changes contributing to poor crop health. Agricultural research has a lengthy history of investigating how management practices impact soil microbiomes and crop productivity, with recent work focusing on plant-associated microbial communities (see refs. <sup>24–29</sup>), however a comprehensive overview of the range of effects across all domains of crop microbiomes is lacking. In addition, a disproportionate amount of research focuses on below-ground sectors of crop microbiomes (soil and root-associated). Far less is known about how management practices shape microbial communities associated with aboveground plant tissues (leaves and flowers) and agriculturally relevant insects. Here we present an integrated view of common themes emerging from decades of research investigating how key management practices alter crop microbiome composition and function (Table 1). We also highlight critical knowledge gaps and areas for further research.

### Agricultural practices can disrupt healthy or native microbiomes.

Agricultural practices are often disruptive for microbial community dynamics because they can alter microbe–microbe interactions and shift the abundance of beneficial (for example, nitrogen fixing or detoxifying) and pathogenic microorganisms predicted to impact

plant health. Chemical inputs and intensification of land use have caused extensively documented negative impacts on crop microbiome structure and function<sup>24–26,30,31</sup>. Although not an agricultural practice, the process of crop domestication also has well-established negative consequences for plant–microbe interactions<sup>32</sup>. In general, three major effects considered harmful to crop-associated microbial communities have been observed: (1) reduced microbial diversity or overall biomass, (2) altered or impaired microbiome functioning, and (3) disruption of beneficial relationships between plant or insect hosts and symbiotic microorganisms.

Although the effects of agricultural practices vary across specific groups of microorganisms, lower overall biomass, species richness and taxonomic diversity are broadly observed in microbiomes associated with repeated use of chemicals to control pests or pathogens<sup>24,25,33</sup>, and in systems dominated by monocultures of one or a few crop species<sup>26,27</sup> or increased soil disturbance resulting from tillage<sup>31,34</sup>. For example, a recent meta-analysis found that conventional tillage reduced soil microbial biomass by more than 30% relative to reduced-till or no-till practices<sup>31</sup>. Soil and foliar pesticide applications can also directly reduce microbial diversity and biomass within crop microbiomes, in some cases decreasing the presence of beneficial microorganisms and causing increases in pathogens<sup>24,25,33</sup>. Furthermore, a recent study found that glyphosate-based herbicide effects can extend beyond soil and phyllosphere communities by affecting relative abundances of gut microbiota in non-target insects that feed on treated plants<sup>35</sup>. However, in many cases it remains unclear whether shifts in microbial diversity and biomass translate to detectable effects on microbiome function. Although the current dogma seems to be that higher taxonomic diversity is beneficial, the extent to which loss of diversity ultimately impacts crop health remains an open question.

On a functional level, various pesticides and some synthetic fertilizers are linked to disruption of soil-nitrifying microbial communities and overall lower metabolic activity<sup>24,25,36</sup>. A recent meta-analysis found that most fungicides broadly inhibit soil microbial growth, reducing microbial biomass by over 50% on average, but variable effects were observed for respiration and nitrogen cycling<sup>33</sup>, which suggests that predicting the effects of management practices on microbiome function will not be straightforward. However, one consistent effect of extensive agrochemical use is enrichment of taxa within microbial communities capable of metabolizing such chemicals. It has long been known that agricultural soils often show higher levels of microbial biodegradation of pesticides<sup>37,38</sup>. Unsurprisingly, enrichment of pesticide-degrading microorganisms in agricultural soils also increases the risk of resistance developing in insect pest populations, particularly for root feeders and species with soil-dwelling developmental stages (see refs. <sup>39,40</sup>). One of the most striking examples of direct microbial detoxification conferring insecticide resistance involves beanbugs and the soil-borne bacterium *Burkholderia*<sup>39</sup>. Repeated insecticide exposure can also rapidly shift the composition of microbial communities associated with insect pests<sup>41</sup>, ultimately enriching for insecticide degraders and reducing taxa that enhance susceptibility<sup>40,42,43</sup>.

Finally, there is growing concern that agricultural practices impair recruitment of beneficial microorganisms mediating important aspects of crop health and agroecosystem functioning<sup>8,44</sup>. The ability of modern crops to sustain relationships or interact with mycorrhizal fungi and plant-growth-promoting rhizobacteria can become compromised during domestication<sup>27</sup>. For example, a comparison of 199 wheat genotypes found root colonization by a beneficial strain of plant-growth-promoting rhizobacteria was substantially higher in ancient genotypes than in modern breeding lines<sup>45</sup>. In addition to domestication, management practices may also alter beneficial crop–microbe interactions. A recent meta-analysis found greater soil disturbance resulting from tillage practices reduces root colonization by beneficial arbuscular

**Table 1 | Summary of positive and negative effects of key management practices on crop microbiomes**

Agricultural practice	Description	Effects on crop microbiomes	References
Chemical control	Application of chemicals to control pests (for example, chewing and sap-sucking insects) and pathogens (for example, harmful viruses, bacteria and fungi) alter microbial community dynamics through direct toxicity and by acting as an energy or nutrient resource. Agrochemicals include herbicides, insecticides, fungicides, nematicides and soil fumigants.	<ul style="list-style-type: none"> <li>↓ Microbial diversity</li> <li>↑ Microbial activity</li> <li>↑ Or ↓ pathogen suppression</li> <li>Disrupts relationships with beneficial microbes</li> <li>Linked to microbe-mediated insecticide resistance</li> <li>Altered microbial functioning</li> </ul>	Soil and rhizosphere <sup>24a,25a,28,33a,69a</sup> Pest insects <sup>40-43</sup> Beneficial insects <sup>53-56</sup>
Crop diversification	Diversification strategies that grow two or more crops in the same location are often designed to improve pest suppression and soil fertility and are thus predicted to alter microbial processes linked to nutrient cycling and pathogen build-up. Practices include crop rotation, cover cropping and intercropping.	<ul style="list-style-type: none"> <li>↑ Or ↓ microbial diversity</li> <li>↑ Soil fertility</li> <li>↑ Disease insect pest suppression</li> <li>↑ Beneficial microbe-plant interactions</li> </ul>	Soil and rhizosphere <sup>26a,27a,30,63-65,68</sup>
Fertilizer inputs	Chemical fertilizers (nitrogen, phosphorus and potassium) enhance crop yield but also alter soil properties (for example, pH) and plant physiology (for example, root exudate production) in ways that are predicted to impact the structure and functional diversity of crop-associated microbiomes.	<ul style="list-style-type: none"> <li>↓ Microbial diversity; varies (for example, soil- versus root-associated)</li> <li>↑ Soil acidification negatively impacts microbial growth</li> <li>↑ Overall microbial biomass; depends on rate and amount</li> <li>↑ Abundance of plant-growth-promoting bacteria</li> <li>↓ Microbial benefits to plant growth with excessive nutrients (for example, N, P and K)</li> </ul>	Soil and rhizosphere <sup>29a,170-175</sup>
Organic soil amendments	Addition of organic matter contributes to soil fertility by enhancing water and nutrient availability to crops, counteracting soil erosion and modulating soil temperature and pH, which in turn are predicted to reshape microbial community structure and function. Examples include compost, manure, biosolids, biochar and plant material residues.	<ul style="list-style-type: none"> <li>↑ Microbial diversity, abundance and metabolic activity</li> <li>↑ Suppression of soil-borne pathogens</li> <li>↑ Positive plant-soil feedback (for example, in maintaining soil structure)</li> </ul>	Soil and rhizosphere <sup>29a,59,61,67,68,168,169</sup>
Tillage	Tillage practices mechanically turn soil as a way to control weeds and pests. However, tillage ultimately causes physical disturbance that leads to changes in soil physiochemical properties and erosion, which in turn are predicted to affect soil microbial communities on many levels.	<ul style="list-style-type: none"> <li>↓ Microbial diversity and overall biomass</li> <li>↓ Microbial functional diversity (for example, catabolic diversity)</li> <li>Disrupts relationships with beneficial microorganisms</li> </ul>	Soil and rhizosphere <sup>31a,34,44a,60,176,177</sup>
Water management	Water can strongly influence soil microorganisms directly or through effects on soil structure and physiochemical properties such as pH. Management of soil moisture through irrigation practices is therefore predicted to influence soil and rhizosphere microbiome communities.	<ul style="list-style-type: none"> <li>↓ Associations with beneficial root microorganisms</li> <li>↓ Presence of water-stress-tolerant microorganisms</li> <li>↑ Multidrug-resistant bacteria in soil (for example, wastewater irrigation)</li> <li>↑ Microbial activity</li> </ul>	Soil and rhizosphere <sup>178-181</sup>

<sup>a</sup>Indicates review or meta-analysis. Up and down arrows indicate increasing and decreasing effects, respectively.

mycorrhizal fungi (AMF) by approximately 30% (ref. <sup>44</sup>). Agrochemical applications, including fungicides and chemical soil disinfection used to suppress microbial pathogens, can also unintentionally weaken plant health by disrupting natural pathogen suppression by microbial competitors, altering nutrient cycling or decomposition processes<sup>46-48</sup>, and may even impact pollination services through effects on floral microbiomes<sup>49</sup>. In fact, studies show pesticides can inhibit or reduce naturally occurring and commercially used biocontrol microorganisms<sup>50,51</sup>, which in turn is problematic for pest management<sup>52</sup>. In addition, pesticide use is predicted to compromise critical relationships between

microorganisms and beneficial insects, including pollinators<sup>53</sup> and natural enemies used to suppress pest populations<sup>54</sup>. Common pesticides not only alter microbial communities associated with pollinators<sup>53,55</sup>, but are also linked to major colony declines in bumble bees<sup>56,57</sup> and increased disease incidence in honey bees<sup>58</sup>, indicating that pesticide-mediated disruptions to microbiota could have widespread effects on beneficial insects.

**Ecology-guided management supports healthy crop microbiomes.** Thus far, management practices that integrate ecological principles to increase or preserve biological diversity have tended

to improve soil quality and ultimately support functionally diverse crop microbiomes (Table 1). Approaches that increase crop diversity, increase available soil nutrients or generally minimize environmental disturbance have been shown to promote diverse crop-associated microbial communities<sup>26,27,30,31,59,60</sup> that in turn are predicted to benefit plant health through mechanisms such as disease suppression and maintenance of essential symbiotic relationships. However, aside from larger-scale systems (for example, maize, wheat or tree crops) the potential benefits of ecology-guided management practices for crop microbiomes are not well understood in emerging areas such as urban farming, aquaponics and controlled environments. Furthermore, there is a general lack of information on how management practices could be leveraged to improve protection of pollinators and natural enemies via effects on insect-associated microbiota.

Agricultural practices that promote crop diversity (for example, rotations or intercropping) and the use of organic soil amendments (for example, manure or compost) have the most notable benefits for mediating crop health via effects on microbial communities<sup>26,59,61</sup>. Several recent meta-analyses report increases in soil microbial diversity and richness ranging from 3% to 27% when cover cropping or crop rotations are implemented relative to monoculture or soils with less agricultural diversity<sup>26,27</sup>. Using a combination of metagenomic and metatranscriptomic analysis in peanut roots, a recent study found that the benefits of increasing crop diversity extend beyond enhanced rhizosphere microbial diversity to reprogramming of key hormonal pathways regulating growth<sup>62</sup>. Practices that foster crop diversity may also promote microbial colonization of roots by AMF, which can provide a range of benefits to their hosts, including increased nutrient acquisition and stress resistance<sup>44</sup>. A meta-analysis of 54 field studies worldwide found that cover cropping enhanced subsequent AMF colonization of summer cash-crop roots by about 30%, and the effect was greatest when the cover crop itself was an AMF host<sup>44</sup>. In addition, crop diversification and application of organic soil amendments are linked to 'suppressive soils' that provide valuable ecosystem services such as disease, weed and insect pest control<sup>59,63–65</sup>. Agricultural practices supporting a diversity of AMF within crop microbial communities have emerged as being critical in the suppression of soil-borne pathogens, which occurs through mechanisms such as competition for root space and modulation of plant immune responses<sup>63</sup>. Recent work in wheat found that enrichment of disease-protective fungi in rhizosphere communities depended on the type of legume in crop rotation<sup>66</sup>, suggesting that specific plant species or cultivars may optimize disease protection. Finally, soil amendments can promote positive plant–soil feedback by maintaining or enhancing soil structure through changes in the microbial community (for example, increased fungal growth<sup>67</sup> and restoring soil microbial diversity following repeated monoculture<sup>68</sup>).

In some cases, positive effects are observed in response to some agrochemicals. For example, increases in the abundance of microorganisms predicted to compete against pathogens and promote plant growth have been observed in chemically treated soils<sup>69</sup>. Herbicides may also stimulate microbial activity and microbial suppression of soil pathogens<sup>25</sup>, thus potentially indirectly benefiting plant health. Similarly, chemical control could indirectly contribute to changes in plant-associated microbiomes that enhance insect pest protection, but this has yet to be tested. In general, it remains unclear why seemingly opposing effects are observed (for example, both negative and positive effects of pesticides) and what specific factors (for example, crop type and geographic region) contribute to the range of impacts management approaches can have on crop microbiomes (Table 1). Disentangling the interconnected nature of microbiomes will therefore be important for developing ecology-guided management strategies that support agroecosystem health. For example, understanding how management influences the phyllosphere

microbiome is critical because it is the aboveground interface between crop plants, insect pests and foliar pathogens. Steering crop microbiomes through management will probably rely on continued efforts to identify unintentional or off-target effects and integration of microbiome knowledge into decision-making.

### Approaches for managing agricultural microbiomes

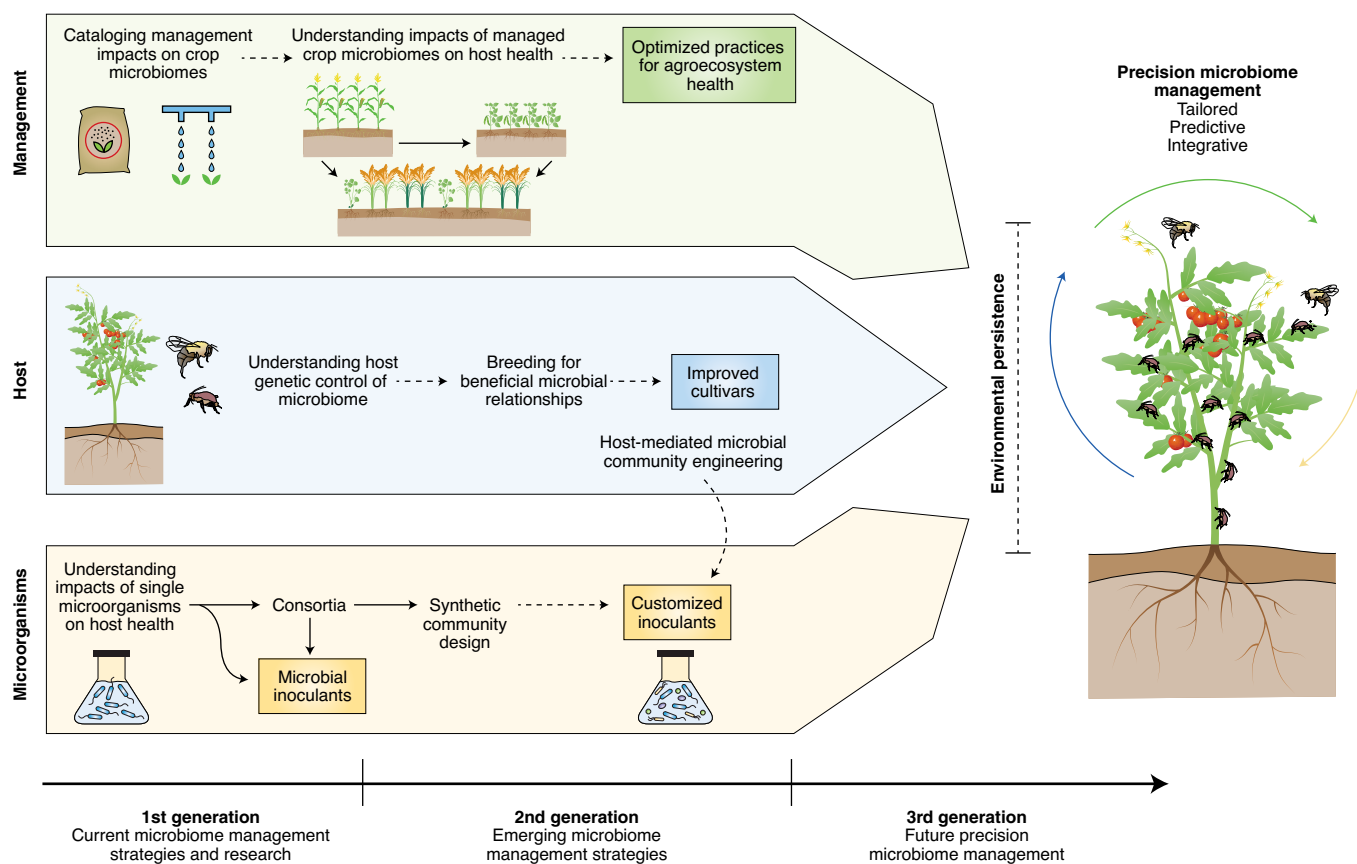
Thus far, intentional microbiome manipulation in agroecosystems has focused on applying single microorganisms to improve plant growth or control pathogens and pests (first-generation microbiome manipulation; Fig. 2), but numerous challenges have prevented their widespread success. In this section, we review the use of first-generation microbial inoculants. We next identify limitations and potential solutions to first-generation microbiome manipulation. Finally, we summarize emerging work that attempts to incorporate more holistic approaches to engineering whole microbial communities and novel approaches to breeding crop plants for enhanced interactions with beneficial microorganisms (second-generation microbiome manipulation; Fig. 2).

**First-generation microbiome manipulation.** Applications of beneficial microorganisms for promoting plant growth or protection from pests and pathogens have been used in agriculture for more than 100 years, beginning with Nitragin, nitrogen-fixing *Rhizobium* spp. for legumes<sup>70</sup>, first patented in 1896. Today, the most commonly used microbial inoculants in agriculture include rhizobia<sup>71</sup>, arbuscular mycorrhizae<sup>72</sup>, free-living nitrogen fixers<sup>73</sup>, entomopathogens<sup>74</sup>, fungal endophytes<sup>75,76</sup> and plant-growth-promoting rhizobacteria<sup>14</sup>. These single-microbe-based products are formulated for delivery by seed treatment or soil drench for soil-dwelling or endophytic organisms, or foliar spray for phyllosphere dwellers<sup>77</sup>. Products can promote plant growth through various mechanisms, including increased nutrient availability or hormone modulation<sup>77</sup>. Biocontrol agents target pests and pathogens directly through competition, hyper-parasitism and other forms of antagonism or indirectly by triggering defence-hormone-mediated systemic resistance<sup>77</sup>. However, even among microorganisms forming tight symbiotic associations with plants or insects (for example, legume–rhizobia, root–mycorrhizae or lactic acid bacteria–insect gut associations), the beneficial effects of single microbial inoculations on host health are variable<sup>71,72,78</sup>. For example, a recent meta-analysis found that effects of rhizobial inoculants on soybean yield ranged from –34% to 109% in the field, depending on presence of native rhizobia, soil characteristics, climate and soybean genotype<sup>71</sup>. In general, microorganisms found to promote growth or control pathogens and pests in laboratory and greenhouse settings often do not provide the same benefit in the field<sup>79</sup> (reviewed in refs. <sup>14,16,77</sup>).

*Overcoming challenges of first-generation microbiome manipulation.* Failure to transfer microbial benefits from controlled conditions to a complex agricultural setting arises due to a number of factors, including lack of correlation between *in vitro* and *in vivo* activity<sup>14,80</sup>, variation across plant genotypes<sup>71,73,75,81–83</sup>, product formulation issues<sup>77</sup> and low environmental persistence<sup>77,79</sup>.

Persistence in the environment is one of the biggest constraints to the effective development of microbial inoculants. Many microbial inoculants provide benefits under controlled conditions with high inoculation rates but fail to persist in the field, leading to low efficacy<sup>77,79</sup>. Often, these inoculants are simply outcompeted by native microbial communities, disappearing within weeks or persisting at low, but ineffective, levels<sup>84–86</sup>. Additionally, the presence of closely related microorganisms in the field may prevent establishment or diminish the effectiveness of an added beneficial microorganism<sup>71</sup>. For example, rhizobial inoculants enhance soybean growth best in fields with a low presence of native rhizobia, suggesting that native strains may competitively exclude the inoculant or that rhizobial





**Fig. 2 | The future of microbiome-informed management requires integration of management practices, host-specific factors and customized microbial biotechnology.** Current progress and areas needing additional research are organized into a projected timeline (for example, generations) that advances towards precision microbiome management. Text in boxes reflects endpoints and products within each area. Solid arrows represent areas of past and current research, and dotted arrows reflect areas of future research. All factors (management, host and microorganism) must overcome the environmental-persistence hurdle, highlighted with a vertical bar, in order to achieve precision microbiome management.

benefits are already maximized in fields with high levels of native strains<sup>71</sup>. Further research is needed to understand how environmental factors (such as native microbial communities, soil type, nutrient levels, environmental stress and management history) influence the establishment of microbial inoculants and benefits conferred to the host under complex field conditions<sup>72,73,87</sup>. In particular, understanding how native microbial communities interact with introduced microorganisms may yield important insights into better management of microbiomes through **inoculative methods**.

Proposed strategies for overcoming environmental-persistence issues include improving methods of strain selection<sup>14,80</sup>, repeated applications<sup>88,89</sup>, and using endophytically colonizing<sup>75,76</sup> and regionally adapted microorganisms<sup>71,90</sup>. Recent work has begun to identify how interconnections between plant- and insect-associated microorganisms might be exploited for improved microbial applications. For example, many insect pathogens colonize plants as endophytic commensals, thus providing the opportunity for pest protection through inoculation of plants, rather than through direct application to invading pests<sup>76</sup>. Additionally, novel strategies to use pollinators for disseminating biocontrol strains<sup>89</sup>, or seed-colonizing endophytes<sup>91,92</sup> to target crop flowers, also show promise. **Genetic engineering to improve beneficial microbial traits has also been heavily researched over the past 30 years<sup>74,93,94</sup>; however, the risks associated with releasing genetically modified microorganisms into the environment are substantial and severely limit their applicability. Efforts to engineer beneficial traits into obligate insect symbionts are more promising, as containment is less of an issue<sup>95</sup>.**

Another approach to optimizing the impact of microbial inoculants involves the development of products containing multiple microbial strains with different functions (for example, plant-growth promotion or biocontrol) that are hypothesized to act additively to **improve plant health**. Several products have been developed using this strategy, but with mixed results<sup>96–99</sup>. For example, increased diversity of *Pseudomonas* strains introduced to alfalfa rhizospheres resulted in community collapse from increasing antagonistic interactions<sup>97</sup>, whereas higher diversity of biocontrol *Pseudomonas* strains introduced to tomato rhizospheres was linked with better persistence, higher suppression of *Ralstonia solanacearum* pathogen populations and reduced bacterial wilt disease symptoms<sup>98</sup>. **Recent modelling suggests that potential negative interactions between different microorganisms could interfere with desired benefits<sup>100,101</sup>.** Additionally, recent work suggests that first-generation microbiome manipulation may be more effective under stressed conditions (that is drought, heat and salinity)<sup>87,102,103</sup>, although additional fieldwork is needed to confirm this.

Not all microbial inoculants need to be persistent to be effective. For example, the pathogen *Erwinia amylovora*, the causal agent of fire blight, has been successfully controlled in apple orchards with yeast (*Aureobasidium pullulans*) and bacterial (*Pantoea agglomerans*) isolates that colonize flowers and prevent the pathogen from establishing<sup>104,105</sup>. In this case, successful control of *Erwinia amylovora* is probably attributable to a relatively small window for infection, and thus long-term persistence of biocontrol inoculants in the environment is unnecessary. Another strategy to

circumvent environmental-persistence issues involved in using bio-control microorganisms is rotation with conventional fungicides, which also reduces levels of synthetic inputs and the risk of fungicide resistance<sup>106,107</sup>. Repeated applications coupled with fungicide rotations can obviate the need for long-term persistence of the bio-control agent.

**Second-generation microbiome manipulation.** Efforts to optimize microbial inoculants may improve their efficacy, but failure to account for complex microbial community interactions has severely limited the success of intentional microbiome manipulation. Thus, to improve management strategies for agricultural microbiomes, microbe–microbe and host–microbiome interactions must be considered. Current efforts to identify positive microbe–microbe interactions contributing to plant health—such as helper bacteria *Delftia* and *Azospirillum* that improve nodulation of rhizobia in the field<sup>108,109</sup>—are promising, although even these effects can be host-genotype dependent<sup>109</sup>. Recent studies have identified beneficial consortia through isolation and identification of synergistic combinations of prevalent community members present in plants grown in disease-suppressive soils<sup>110,111</sup>. In one study, a consortium of several native isolates reduced plant mortality by half in a field setting<sup>111</sup>, and these isolates were recovered at the end of the field season, suggesting that this approach may be effective in identifying and deploying persistent microbial consortia in large-scale crop protection. However, identification of properties of highly complex communities that can be used to rationally design microbial consortia to perform specific functions that benefit crop health remains difficult. The following section summarizes recent efforts to develop methods for engineering beneficial crop microbiomes from a community perspective. In addition, we discuss progress towards breeding crops for beneficial interactions with entire microbial communities.

**Designing synthetic communities.** One promising avenue for whole-microbiome manipulation is the design of synthetic communities using culturable isolates to reconstitute a simplified microbiome in structure and function<sup>14,15,112–114</sup>. Thus far, this approach has primarily been used to understand basic features of microbial community assembly and functional interactions. Predicting higher-order community dynamics has proven challenging<sup>115</sup>, although measuring the effects of a subset of all possible pairwise combinations enabled the development of a predictive model capable of identifying combinations of bacteria with predictable effects on plant responses<sup>116</sup>. Advances in high-throughput screening technologies will also enable faster identification and improved design of beneficial consortia<sup>117</sup>. While further research will probably improve the effectiveness of the inoculation approach to developing beneficial microbial consortia, additional microbiome-manipulation approaches are needed for different farming systems. Recently, researchers have proposed alternative microbiome-manipulation strategies, including ‘steering’ native microbiomes towards a desired beneficial outcome<sup>118,119</sup> using host-mediated engineering and crop breeding for positive microbiome interactions. These two approaches are reviewed below.

**Host-mediated engineering of microbiomes.** Host-mediated engineering refers to the use of a host organism (for example, a plant or animal) to selectively generate microbial communities that produce desired effects on specific host traits (for example, on stress resistance, growth and reproduction)<sup>119</sup>. This process was originally demonstrated in *Arabidopsis* plants by Swenson et al.<sup>120</sup>, where selection for a growth-promoting soil biotic community successfully increased plant biomass. Host-guided engineering efforts have since focused on abiotic stress tolerance and phenology (that is, flowering time and hatching time) in wheat<sup>121</sup>, *Arabidopsis*<sup>122</sup> and

the fruit fly<sup>123</sup>. Additional traits known to be modulated by microorganisms are promising candidates for host-mediated selection on rhizosphere and phyllosphere-associated<sup>124</sup> crop microbiomes, such as growth, development and various stress responses. Engineering robust colonizing leaf or endophyte microbial communities that directly alter insect health—whether positively in the case of beneficial insects like pollinators, or negatively for pest insects—may also be possible using host-mediated selection approaches<sup>119,125</sup>.

One of the major benefits of host-mediated engineering is that it does not rely on a specific mechanism or function associated with the target microbiome. Instead, by selecting for a desired host trait associated with a particular microbial community, antagonistic interactions between microorganisms can be avoided and more stable communities may evolve over time<sup>119,124</sup>. However, many outstanding questions remain for optimization and successful implementation of host-mediated selection, including choice of host trait, strength of selection to impose on the target microbial community, transferability and stability of the selected microbiome, appropriate experimental controls, and competing sources of environmental selection that could interfere with beneficial effects of engineered microbiomes. In addition, current host-engineering experiments have been performed under highly controlled conditions and further work is required to determine whether selected microbiomes are effective under field conditions given the enormous variation in soil type, native microbial communities and climate. Overall, methods aimed at selectively engineering microbial communities require substantial further research before being applied to agricultural crops and insects.

**Breeding for beneficial plant–microbe interactions.** Natural variation in microbial community composition and responsiveness to introduced microorganisms has been shown for many crop plants, including common bean<sup>126</sup>, maize<sup>127,128</sup>, rice<sup>129,130</sup>, barley<sup>83</sup> and tomato<sup>82,131</sup>, with plant cultivar contributing to 5–20% of overall microbiome variation. Many of these studies examined variation in microbiome composition and diversity across a small number of genotypes and growing conditions, which limits the ability to generalize genotypic effects on the microbiome. Large-scale field studies examining heritability of the root-associated microbiome have been performed only for maize<sup>127,128</sup> and rice<sup>130</sup>, although overall, it is largely unclear whether and how heritable variation in the microbiome correlates with beneficial traits.

The next step towards developing crop breeding that integrates knowledge of microbiomes is to identify target traits for beneficial plant–microbe interactions. Although several studies have identified natural variation for recruitment of beneficial bacteria to roots<sup>81,82,131,132</sup>, few loci related to microbiome-related traits have been isolated. As domestication appears to have limited the ability of modern cultivars to interact with beneficial microorganisms, some researchers suggest mining wild relatives of modern crops for beneficial microbe–plant interaction traits<sup>18,133</sup>, which has resulted in identification of a beneficial allele of the *OsCERK1* locus in wild rice that enhances AMF colonization in roots when expressed in cultivated rice varieties<sup>129</sup>. The plant immune system has also been implicated in proper root endosphere microbiome assembly<sup>134</sup>; thus, it has been hypothesized that genetic variation in plant defences may contribute to interactions with the rhizosphere microbiome<sup>126,135</sup>. To date, this hypothesis has primarily been tested in the model plant *Arabidopsis thaliana*<sup>81,136</sup>. For example, natural variation in root-specific production of the natural antimicrobial camalexin has been shown to be positively correlated with response to growth-promoting bacteria such as *Pseudomonas* CH267 (ref. 137). Plant signalling pathways that function in communication with microbial communities are only beginning to be explored<sup>83,136,137,138</sup>. Continued focus on this area will vastly increase our ability to identify and deploy microbiome-related traits in crop breeding.

Thus far, efforts to genetically engineer plants to alter relationships with microorganisms have focused on increasing pathogen resistance<sup>139</sup> and introducing nitrogen fixation<sup>140</sup>. More recently, RNA interference targeting obligate insect symbionts has been engineered into host plants to control pests<sup>141–143</sup>. Gene-editing strategies such as clustered regularly interspaced short palindromic repeats (CRISPR) have been used to improve host resistance to pathogens and pests<sup>139</sup> and accelerate domestication of wild crops<sup>144–146</sup>, which could be used in reverse to reintroduce beneficial microbiome-related traits from wild relatives. Plant genetic modification, while more difficult to perform than microbial genetic modification, is more straightforward from a regulatory standpoint, although regulatory and social hurdles to crop genetic modification remain considerable. Novel strategies are being developed to co-engineer plants and microorganisms<sup>147</sup>, laying the groundwork for engineering plants able to attract or activate co-engineered beneficial microorganisms through an artificial plant-generated signal and microbial response. This approach could potentially alleviate both the persistence problem of microbial inoculants as well as concerns over containment of genetically modified microorganisms by combining signal recognition with strategies for containment.

A major challenge for breeding microbiome-related traits is the potential for off-target or undesirable side effects on host fitness and microbial community dynamics. For example, increased recruitment of beneficial *Pseudomonas* isolates in *Arabidopsis* roots incurred the cost of greater susceptibility to *Pseudomonas syringae*<sup>81</sup>. In addition, breeding for beneficial plant–microbiome traits faces the same challenges as all quantitatively variable traits, namely difficulty in breeding of many quantitative trait loci with small effects. Nevertheless, even if traditional breeding for beneficial traits is not feasible, an increased understanding of genotypic variation in beneficial microbiome-related traits will improve cultivar selection, and novel gene-editing techniques will enable targeted alterations that enhance beneficial interactions with microbial communities.

### The future of precision microbiome management

After decades of research on crop-associated microbial communities, the path towards effective microbiome-informed management is taking shape. Application of ecological concepts targeting community-level properties of microbiomes rather than single microorganisms shows the most promise for enhancing crop protection and improving sustainability. However, the combination of techniques that prove most effective for promoting beneficial crop microbiomes will likely depend on climate and soil conditions specific to geographic regions and the unique attributes of different farming systems. Embracing the complexity and interconnected nature of agricultural microbiomes will be critical for establishing the knowledge base needed to develop management options that maximize microbial benefits to crop health and advance microbial biotechnology.

In parallel with incorporation of the human microbiome in development of precision medical treatments<sup>148</sup>, the path forward for agriculture is to create individualized management plans that include all interconnected sectors of crop microbiomes (Fig. 1). Thus far, crop-associated microbiome data have largely been left out of the framework for advancing precision or digital agricultural approaches, although the possibilities are beginning to be recognized<sup>15,149</sup>. The future of precision microbiome management will therefore customize management practices, host-specific factors and microbial biotechnology (Fig. 2, 3rd generation) to promote both crop health and agroecosystem sustainability. Importantly, this next generation of microbiome-informed management must extend not only to field crops, but also to the growing sectors of controlled-environment agriculture (that is, greenhouse, urban agriculture and hydroponics).

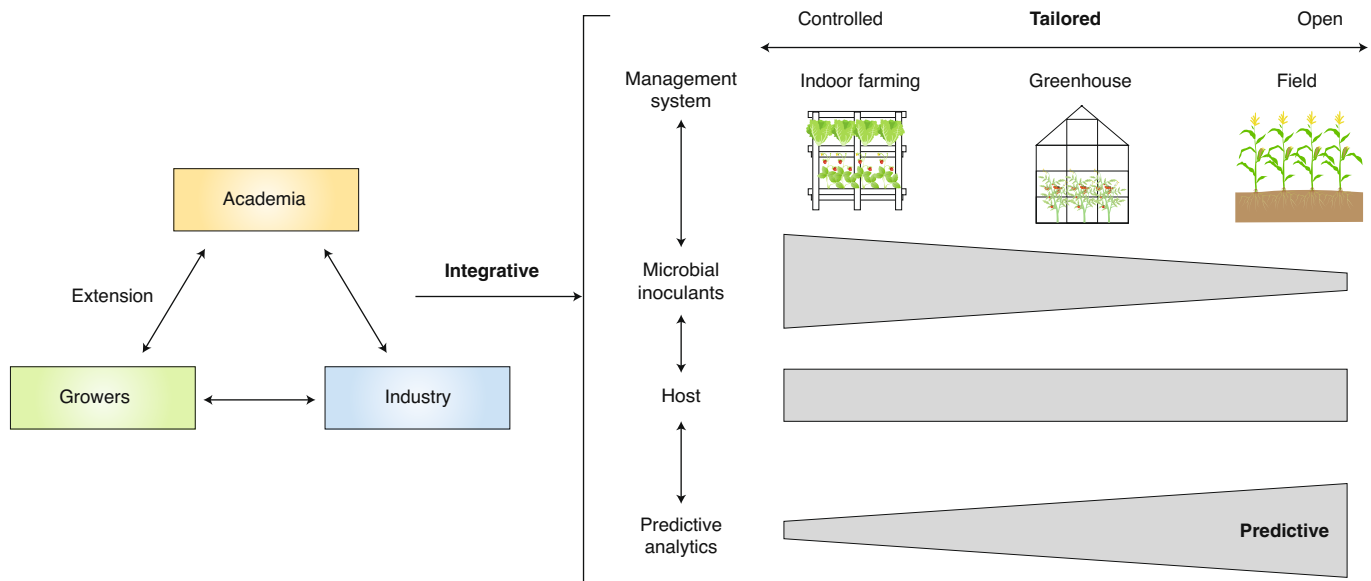
The next steps towards translation of crop microbiome knowledge for enhanced crop protection and performance across diverse

farming systems will require approaches that are tailored, predictive and integrative (Fig. 3). Tailoring microbiome-based management solutions to different farming systems will depend on a number of different farming system characteristics (for example, conventional versus organic practices, controlled environment versus field system and size). For example, beneficial microbial inoculants often improve plant growth and protection under controlled laboratory or greenhouse conditions, in contrast to variable success of applications under field conditions. Single-microorganism inoculants may therefore be more useful under controlled settings, such as indoor agriculture, hydroponics, aquaponics and high tunnels. It may even be possible to use genetically modified microbial inoculants in controlled-environment agriculture, given appropriate containment and cost-effectiveness. By contrast, large-scale conventional commodity crop farms may benefit more from predictive analysis that enables regionally customized management to steer the microbiome than from microbial inoculants, although further research may improve the use of inoculants in field crops. Within-field data on a multitude of yield parameters already exist for field crops (precision farming); integrating microbiome data into this framework will likely enable the discovery of predictive metrics for soil health, crop yields and disease severity<sup>150</sup>. Finally, third-generation microbiome management will require integration across all three sectors of microbiome research: management, host, and microbial biotechnology (Figs. 2 and 3).

### Critical research needs for managing crop microbiomes.

*Capitalizing on interconnectedness of plant, soil and insect microbiomes to develop novel microbial biotechnology and improve management practices.* There is a general lack of information on microbiomes of agriculturally relevant insects and aboveground plant tissues (for example, leaves, flowers and pollen) relative to existing knowledge of soil microbial communities (see Table 1). Filling these knowledge gaps will enable development of novel microbial inoculants that take advantage of the intersection between plant and insect microbiomes; for example, through development of stable consortia that provide multiple simultaneous benefits, such as protecting from foliar pathogens and improving pollinator health. In fact, research in strawberry indicates that rhizosphere microorganisms not only move into aboveground plant tissues (such as leaves and flowers) where they can be transferred between plants by pollinators, but some strains can also form mutualistic relationships that protect both plants and pollinators from pathogens<sup>21</sup>. The floral microbiome is generally understudied, but has important implications for pollinator health and understanding how management practices shapes crop plant–pollinator interactions<sup>151</sup>. Additionally, although microbial symbionts are hailed as the next generation of insect pest control, we know very little about how management practices alter insect microbiomes. Do insecticides and crop-diversification practices affect microbial communities of insect vectors and thus transmission of plant pathogens in agricultural landscapes? Could chemical control practices induce systemic changes in phyllosphere or rhizosphere communities that indirectly affect pest resistance or attractiveness to pollinators? Overall, more research is needed that investigates how management practices alter complex relationships between plants, insects and microorganisms.

*Identification and development of synergistic management practices that positively steer the microbiome to improve crop protection and overall production.* Interacting or synergistic effects of agricultural practices and microbial biotechnology on microbiome structure and function are not well studied. For example, a growing body of work indicates that crop-diversification practices promote higher soil microbial diversity; however, additional practices (for example, tillage or chemical control) could counteract potential benefits for crop health (Table 1). Furthermore, management practices can



**Fig. 3 | Third-generation microbiome management will be tailored across different farming systems, use predictive analytics to optimize management, and integrate across management, microbial biotechnology and host genetics.** Achieving third-generation microbiome management will require extensive collaboration across academia, industry and growers with extension serving as an essential mediator among these groups. Grey bars indicate hypothesized relative importance of each area along the continuum of farming systems from controlled to open. Microbial inoculants may be more useful under controlled growing conditions, whereas predictive analytics for microbiome management may be more useful for large-scale field agriculture.

generate variable effects across crop microbiomes, depending on microbiome source (for example, soil versus rhizosphere), group of microorganisms (for example, bacteria versus fungi), soil type or existing native communities, and may produce only minor impacts relative to additional dominant factors shaping microbial communities (for example, plant growth stage, species, cultivar, climate, or weather variables). Researchers are only beginning to document how the multiple interacting layers of management translate to changes in crop health and productivity. It will therefore be important for future work to identify when management leads to conflicting effects and how to avoid detracting from beneficial plant–microbe relationships, particularly when integrating microbial biotechnology. Intentional use of key practices (such as crop rotations and organic amendments) to steer microbial communities to produce specific outcomes for crop health is not well documented. For example, although positive plant–soil feedback leading to suppression of insect pest populations has been confirmed in greenhouse and laboratory studies<sup>152,153</sup>, how field-management practices could be designed to produce similar effects is unclear. Further knowledge of processes governing microbial community stability and evolution is needed, which will in turn contribute to the effectiveness and persistence of introduced microbial products.

*Continued improvement of first-generation and validation of novel second-generation microbial biotechnologies in large-scale agricultural contexts.* Although microbial inoculants have been used in agriculture for the past 100 years, much remains to be accomplished for their full integration as a standard agricultural practice, in particular overcoming persistence in the field, one of the major hurdles to inoculant effectiveness. Further work in understanding interactions between introduced inoculants and native communities, identifying microbe–microbe interactions important to emergent host phenotypes and community stability, and developing best practices for introducing engineered communities—whether through synthetic community inoculants or through soil-transplant methods<sup>118,154</sup>—will facilitate improved effectiveness of microbial inoculant biotechnology. Novel approaches to identifying

microbial traits important to plant health in the field, coupled with high-throughput screening<sup>155</sup>, will also enable discovery and implementation of improved biotechnology.

*Identification of beneficial microbiome-related crop traits for both traditional and next-generation gene-editing-assisted breeding.* Disentangling the complex chemical communication between plants and associated microbial communities is an emerging area of research<sup>83,136,137,138</sup> that will allow for the identification of plant genetic traits that underlie host–microbiome interactions. Identifying these microbiome-related traits will enable breeding efforts that take advantage of the extended genome of plants<sup>11</sup> through both traditional breeding methods as well as through transgenic and gene-editing techniques. Combining emerging technologies, such as experimental microbial ecosystems used for precise manipulation of root microbiomes (for example, EcoFABs<sup>156</sup>) and high-throughput automated sensing platforms for plant phenotyping (that is, phenomics), could further enable researchers to screen for microbiome-related host phenotypes to assist breeding efforts, as well as design and test microbial products to optimize beneficial plant–microbial partnerships. Development of EcoFABs for identifying microbiome-related crop traits is promising, but the scale of these systems is currently limited and thus not yet applicable to the interaction between microbiome and the whole plant or non-model species.

*Development of predictive analytics and modelling integrated with precision management.* There remains a complete lack of methods to predict the effects of management on the structure and function of crop microbiomes. However, a recent study using a phylogenetic approach found that soil microbial communities are compositionally more similar between close plant relatives, suggesting that the impact of crop rotation practices on structuring agricultural soil microbiomes can, in part, be predicted by crop species and relatedness<sup>157</sup>. Initial efforts to use spatial variation in microbiome data to predict crop and pollinator health are also promising<sup>150,158–160</sup>, but need to be validated with larger sample sizes across diverse



agroecosystems. The incredible heterogeneity of microbial communities due to differing soil conditions even within the same field will probably complicate these efforts<sup>8,160,161</sup>. However, new technology enabling inexpensive, high-throughput quantitative PCR<sup>162</sup> and automated, consistent soil sampling will probably make quantitative monitoring of agricultural-productivity-associated bacterial taxa or functional genes financially and technically feasible. However, predictive microbiome management at field scale will require advances in computational approaches that can translate increasingly large amounts of microbiome data into data-driven decisions for managing all interconnected sectors of crop microbiomes, such as risk assessment, use of microbial indicators to identify stress or damage, and predictive modelling of microbiome spatio-temporal dynamics.

*Identification of best practices in microbiome management for different farming systems.* Not only is there a general need to evaluate the effectiveness of microbial biotechnology and management approaches in emerging farming systems (for example, urban, aquaponics and controlled-environment systems), but incorporating unique attributes of each system will be important for establishing best practices. For example, differences between annual and perennial systems may make crop microbiomes more or less amenable to manipulation due to differences in breeding cycles. Effectiveness of microbial biotechnology may therefore rely on repeated application in annual crops, whereas the roots of perennial crops (for example, bioenergy, forage and tree crops) may be able to maintain beneficial consortia over multiple growing seasons. Another key to developing customized microbiome management in different farming systems will be determining to what extent microbial diversity is a good indicator and overall driver of crop health and agroecosystem function. Should diversity be a target for managing crop microbiomes or engineering of microbial community inoculants, and if so, what balance of functional and taxonomic diversity should be maintained? Lower diversity is not always indicative of unhealthy or unstable microbial communities<sup>163</sup>, and in some cases efforts to manage microbiome diversity have resulted in community collapse from increasing antagonistic interactions<sup>97</sup>. Learning from studies in natural or unmanaged systems will be important for expanding basic theory on microbial community dynamics and applying community ecology concepts that promote crop health and agroecosystem functioning, without being overly reliant on measures of diversity<sup>164</sup>. Finally, the short-term versus long-term effects of reshaping microbiomes through agricultural practices and use of microbial biotechnology is underexplored. Some practices exhibit high but transient effects on microbial communities (see refs. <sup>165–167</sup>), suggesting that crop microbiomes may recover from disturbances. Conversely, long-term organic management is linked to higher soil and rhizosphere microbial diversity<sup>168,169</sup>, which in turn has been shown to promote resistance to insect pests<sup>153</sup>. However, it is generally unclear how to optimize management practices and microbial technology to boost crop production, while also avoiding physiological trade-offs and maintaining long-term agroecosystem sustainability.

### Concluding vision

A one-size-fits-all approach to managing agricultural microbiomes is unrealistic. There is a clear need for improved integration of microbial technology and host genetics to develop best management practices that are optimized across diverse farming systems. The current disconnect between industry production of next-generation microbial products and research supporting the benefits of commercially available products under variable conditions will be a challenge to navigate. Advancing precision microbiome management will therefore require coordination across academia, industry, growers and the public. Furthermore,

translation of microbiome research relies on engagement and education efforts to bridge gaps and disseminate information tailored to the needs of different growers. Interdisciplinary training of scientists and integrated research efforts across academic–industry–grower partnerships will be needed, as well as further development of data-collection technology (for example, sensors and drones) in order to identify and deploy the best strategies for microbiome management. Agricultural microbiome management is complex and multifaceted, but by addressing critical research needs, appropriate guidelines and approaches can be developed. We ultimately envision a decision-tree framework that will enable growers to make data-driven management decisions on the appropriate practices, cultivars and microbial inoculants to optimize the health of their crop and soil for their specific region and farming system. These are exciting times for harmonizing efforts that harness the power and complexity of all interacting sectors of crop microbiomes to fuel a future of sustainable and healthy agroecosystems.

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## Author contributions

E.F. and L.E. conceived and wrote the manuscript. A.I.-P., I.K. and C.H.N. provided conceptual guidance, contributed the body of literature reviewed and edited the manuscript.

## Competing interests

The authors declare no competing interests.

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