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Review

Agriculture and the Disruption of Plant–Microbial Symbiosis

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Domestication has transformed hundreds of wild plant species into productive cultivars for human utility. However, cultivation practices and intense artificial selection for yield may entail a hidden cost: the disruption of interactions between plants and beneficial microbiota. Here, we synthesize theory predicting that evolutionary trade-offs, genetic costs, and relaxed selection disrupt plant–microbial symbiosis under domestication, and review the wealth of new data interrogating these predictions in crops. We describe the agronomic practices, ecological scenarios, and genomic attributes that can result in the disruption of symbiosis, and highlight new work probing its molecular basis. To improve agricultural output and sustainability, research should develop breeding methods to optimize symbiotic outcomes in crop species.

Highlights

Many crops interact differently with beneficial microbiota compared with their wild relatives.

Plant traits that regulate symbiosis can be disrupted because: (i) disruption of the trait is favored directly or indirectly by artificial selection; (ii) plant traits accumulate deleterious genetic mutations due to the demographics of the breeding population; or (iii) disruption of the trait is selectively neutral under agricultural conditions.

These mechanisms generate distinct patterns of symbiosis trait evolution, each of which can be detected with trait-based and population-genetic analysis.

Identifying mechanisms that result in symbiosis trait disruption in crops will be essential for future efforts to maximize the benefits of microbial symbiosis for crops.

The Disruption of Symbioses in Domesticated Plants

Humans have reshaped the biosphere, driving rapid evolution in the species that we exploit [1]. Agriculture stands out as a vast human alteration of biodiversity on Earth: over 12 000 years, humans have molded hundreds of wild plant species into productive crops [2] that cover >35% of the terrestrial habitat [3]. Domestication is a multistaged response to human-imposed selection that progresses from the increase in frequency of desirable alleles in nearly wild populations, to the formation of cultivated populations and deliberate breeding and improvement [4]. Breeding practices have favored crop lineages that produce large, flavorful, and rapidly growing vegetative structures, fruits, and seeds, with improved disease resistance and environmental tolerance traits that manifest primarily in aboveground plant tissues [2]. However, belowground traits can be difficult for humans to evaluate during domestication and crop improvement [5]. Thus, the evolutionary **disruption of plant–microbe symbioses** (see Glossary), that is, a decrease in the interaction of crops with beneficial soil microbiota [6–8], can go undetected.

Over the past century, research on global staple crops and their associations with microbes has increased considerably. For example, the proportion of papers on agricultural staple crops with symbiosis or inoculation in the topic has nearly doubled since 2000 (Figure S1 in the supplemental information online). Seminal work on wheat (*Triticum aestivum*) [9–11] and soybean (*Glycine max)* [7] reveals different outcomes of microbial symbiosis between modern cultivars and their less domesticated or wild ancestors, with modern crops being less responsive to symbionts and exerting less robust partner choice. However, measures of symbiotic responsiveness must be viewed cautiously, because data interpreted to indicate that newer cultivars are less able to benefit from symbiosis [9] can be driven by changes in plant performance in the symbiont-free state [12], as explained in Box 1. New research has expanded to diverse crop lineages, showing that reductions in **symbiosis traits** can be linked to evolutionary changes in plants that occur during domestication [8,13–15]. Symbiosis traits regulate microbial colonization and infection, and can encompass a range of plant phenotypes and mechanisms, from structures in roots and other tissues that host microbes, to the molecular and physiological systems that regulate them (Box 2).

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In natural populations, **beneficial microbes** are defined by their ability to generate fitness benefits for hosts that outweigh investments hosts pay to engage in symbiosis. The net benefit for a plant from a microbial symbiont will decrease if the resource a symbiont provides becomes freely available in the environment, as can occur in agriculture. Many fungal and bacterial plant symbionts, ranging from endophytes to epiphytes, are not well characterized. Thus, here, we focus on model plant symbioses with arbuscular mycorrhizal fungi (AMF) and root-nodulating bacteria (rhizobia) to provide examples for broader and likely more complex phenomena in

Box 1. Quantifying Plant Response to Symbiosis

Responsiveness (R) metrics quantify the impact of symbiosis by comparing plant performance in symbiotic (S) and uncolonized (U) states via their:

difference	$R_1 = S–U$
proportional difference	$R_2 = S/U$
scaled difference	$R_3 = (S–U)/U$,
or log response ratio	$R_4 = \log(S/U)$

Crops could evolve to be larger than wild relatives without a change in R (Figure IA). Crops could evolve lower R if, as they become larger (Figure IB, broken line), they also become less dependent on symbionts (i.e., evolve high performance without the symbiont), or if, as they become larger (Figure IC, broken line), their ability to benefit from symbionts degrades. If S varies little among lineages, but U varies substantially, high R will be driven by lineages with low U [39] and breeding to maximize R could inadvertently select for plants that perform poorly without a symbiont.

To identify plant genotypes that benefit most from symbiosis, genotype values can be used to parameterize a regression to generate residuals for S after accounting for its association with U (Equation I):

$$S = \beta_1 + \beta_2 U + e, \qquad [I]$$

where β_1 denotes the intercept, β_2, the slope of the relationship between S and U, and e, the residual variance [12]. A large residual for a plant genotype indicates that symbiosis has a large impact on performance, given the non-colonized performance of the genotype (Figure ID, red circle). Comparison of wild and domesticated genotypes assumes a consistent linear relationship between S and U among these groups. To investigate genetic bases, both responsiveness values and these residuals can be used in genome-wide association or quantitative trait locus mapping. To test whether groups such as wild versus domesticated genotypes differ in the benefit they receive from symbiosis, linear models of raw performance data could be used to test whether there are group-specific effects of symbiosis.

Responsiveness metrics quantify the magnitude of plasticity in response to symbiosis, whereas these residuals (Figure ID) identify genotypes with unusually large or small S, after accounting for U. Both sources of variance could be important for maximizing symbiosis benefits if breeders can select for plants that gain a high performance boost from symbionts as well as higher fitness in their absence. Understanding whether trade-offs, genetic costs, or relaxed selection drive symbiosis evolution at a physiological or molecular level [39] could help determine whether low responsiveness in crops is an adaptive response to agricultural conditions (Figure IB) or is deleterious (Figure IC).

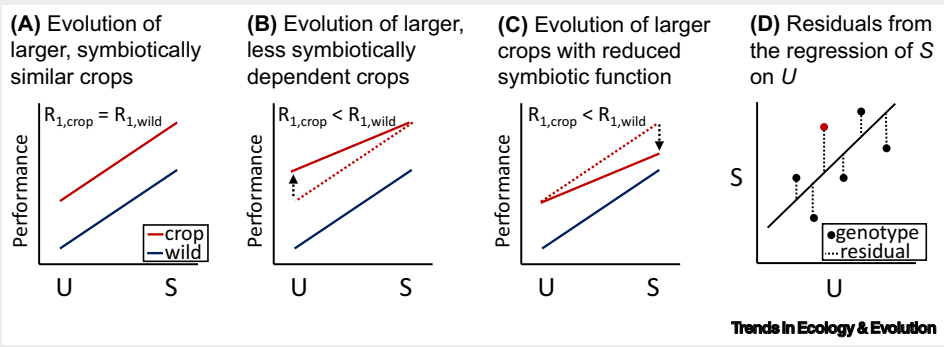

Figure I. Possible Evolutionary Scenarios for Symbiotic Responsiveness (R_1) versus Plant Performance in Symbiotic (S) and Uncolonized (U) Conditions during Domestication.

Glossary

Antagonistic pleiotropy: a scenario in which an allele affects more than one trait, at least one of which improves fitness and at least one of which is deleterious.
Beneficial microbes: host-associated microbes that generate a fitness benefit for hosts relative to hosts lacking the association. Such benefits can be context dependent: a microbe may only increase fitness under conditions where the benefits of microbial resources outweigh costs to the host.
Disruption of plant–microbe symbioses: an evolutionary or ecological decrease in the magnitude of the interaction of plants with beneficial soil microbiota. Reduction of a symbiosis trait could have a deleterious, adaptive, or neutral impact on plant fitness.
Expansion load: expanding populations experience stochastic loss of genetic diversity at their expansion front, thus increasing drift and adding to the burden of deleterious mutations in the population.
Genetic draft: fluctuations in allele frequencies driven by selection on variation at linked loci (i.e., genetic hitchhiking).
Genetic drift: random changes in allele frequencies within a population, usually owing to the chance disappearance of alleles.
Hybrid production: crossing of distinct breeding pools allowing for complementation of negative and/or positive features of parental types.
Introgression: genetic exchange that occurs between different species resulting from hybridization, followed by backcrossing of hybrids with one or both parent species.
Linkage disequilibrium (LD): nonrandom association of alleles from independent loci in a population, usually arising from the inheritance of neighboring alleles that are not separated by recombination.
Positive selection: natural selection that favors an allele, causing that allele to increase in frequency in a population.
Purifying selection: natural selection that disfavors a deleterious allele, causing that allele to be purged from a population.
Ratio of nonsynonymous to synonymous substitutions (d_N/d_S): a parameter that estimates the relative role of **purifying selection** versus **positive**

plant microbiomes. Benefit from costly services, such as phosphorus provisioning (by mycorrhizae) or symbiotic nitrogen fixation (by rhizobia), can be inhibited or negated under fertilization if these nutrients are freely available to plants in the soil [16–18]. Similarly, drought protection offered by rhizosphere microbes can be devalued if irrigation prevents drought stress conditions [19]. Enhanced competitive ability mediated by soil microbiota can be rendered superfluous under herbicide treatments that eliminate weeds [20], and microbe-mediated resistance to herbivores can be devalued if pesticides remove herbivores at no cost to the plant [21]. Modern intensive agriculture succeeds in protecting crops and enhancing yield, but could cause agricultural plants to evolve to shunt resources away from traits that underlie symbiosis. The consequence of the evolution of symbiosis disruption in crops under fertilized conditions depend upon whether such disruption impedes crop performance under lower, more sustainable anthropogenic inputs in agriculture [6,22,23]; thus, symbiotic disruption could be detrimental or adaptive with respect to plant performance, and might depend on local conditions (Box 1 and see Outstanding Questions). Moreover, any negative effects of the disruption of crop symbiosis traits will be compounded if agricultural practices drive declines in the overall level of cooperation in symbiont populations, as explained in Box 3.

Beneficial soil microbiota have tremendous potential to improve plant health and food security. Microbes can improve plant nutrient acquisition, defense, and stress tolerance without the environmental and socioeconomic costs associated with agrichemical inputs [24–26]. Understanding microbial services, the plant phenotypes and molecular mechanisms that

selection acting on a set of homologous protein-coding loci. Synonymous substitutions (d_s) are changes in coding DNA sequences that do not lead to an altered amino acid, and are assumed to be neutral. Conversely, nonsynonymous substitutions (d_N) alter amino acids, and can either be deleterious, neutral, or beneficial, depending on the function of the gene and how the genes expression interacts with the environment.

Recombination: breaking up of linkage between neighboring loci that occurs during meiosis. The reshuffling of alleles that occurs during recombination causes offspring to bear a unique combination of loci relative to parents.

Resource allocation trade-off: a constraint whereby a limited resource must be distributed between competing traits, such as growth versus reproduction.

Symbiosis traits: inherited traits that underlie host responses to beneficial microbes and/or regulate colonization and infection by beneficial microbes. Symbiosis traits encompass a variety of host phenotypes and mechanisms, including tissues that house microbes, signaling molecules that control infection, morphological or chemical traits that alter host benefit from microbes, and physiological and developmental systems that regulate microbial proliferation and transmission.

Box 2. Pathways to Symbiosis Trait Evolution

Plant symbiosis traits regulate the onset, maintenance, and termination of microbial colonization and establishment. The disruption of symbiosis traits describes changes that reduce symbiotic function or the extent to which plants benefit from, are dependent on, or are responsive to symbionts. While some studies find the symbiosis traits of crops and their wild relatives to be indistinguishable (e.g., [94]), we highlight here ways in which such traits can differ.

Canalized versus Phenotypically Plastic Changes in Symbiosis Function

Alleles that decrease the presence or regulation of symbiosis, irrespective of the environment, could lead to canalized disruption. This has occurred over deep evolutionary time: numerous plant lineages have lost the ability to form root nodules or mycorrhizal associations [35,38,95]. More recently, sunflower and breadfruit (*Artocarpus altilis*) cultivars have evolved lower rates of AMF colonization with increased domestication [13,14] (Figure IA,B), and cereal crop cultivars developed after 1950 benefit less from AMF compared with pre-1950 ancestral lineages [15] (Figure IC).

Trait reduction can also vary with the environment via phenotypic plasticity. Under nutrient enrichment, plants can minimize association with microbiota [35,96] and domesticated lineages can adapt to more readily divest from symbiosis in response to the availability of environmental resources. While diverse domesticated and wild crop lineages have indistinguishable growth responsiveness to mycorrhizae in low-phosphorus conditions, under high-phosphorus conditions domesticated lineages can rely more heavily upon environmental phosphorous sources and benefit less from mycorrhizae compared with wild lineages [8] (Figure ID).

Changes in the Initiation versus Functionality of Symbiosis

Initiation of microbial colonization via compatible molecular signaling interactions that prompt the production of structures such as root nodules or mycorrhizal arbuscules often incur a minor cost to a plant. However, the carbon costs of maintaining a functional symbiosis can be substantial [32,97]. These phases of symbiosis can be under distinct genetic controls and could evolve independently. In wheat, both decline: symbiosis initiation (percentage of roots colonized by mycorrhizae) and symbiosis functionality (percent growth increase in response to mycorrhizae) can be higher for older cultivars [9] (Figure IE; but see Box 1 in the main text for caveats). These paths to symbiosis decline differ in impact on symbiont fitness benefits from plants and, thus, the evolutionary trajectory of symbiont cooperation (Box 3).

Changes in Symbiotic Specificity

Symbiotic specificity is a heritable plant trait that can evolve and impact plant performance [86,98]. Consistent with a decrease in specificity with domestication, newer breadfruit cultivars (originating farther from the center of origin for breadfruit domestication in New Guinea) harbor a higher diversity of AMF phylotypes compared with older cultivars [13] (Figure IF). Furthermore, the ability to discern between more and less cooperative symbionts can decline during domestication. Newer soybean cultivars are less able to maintain seed production when presented with a mixture of effective and ineffective rhizobia, suggesting that they are also less able to preferentially allocate resources to superior symbionts [7] (Figure IG).

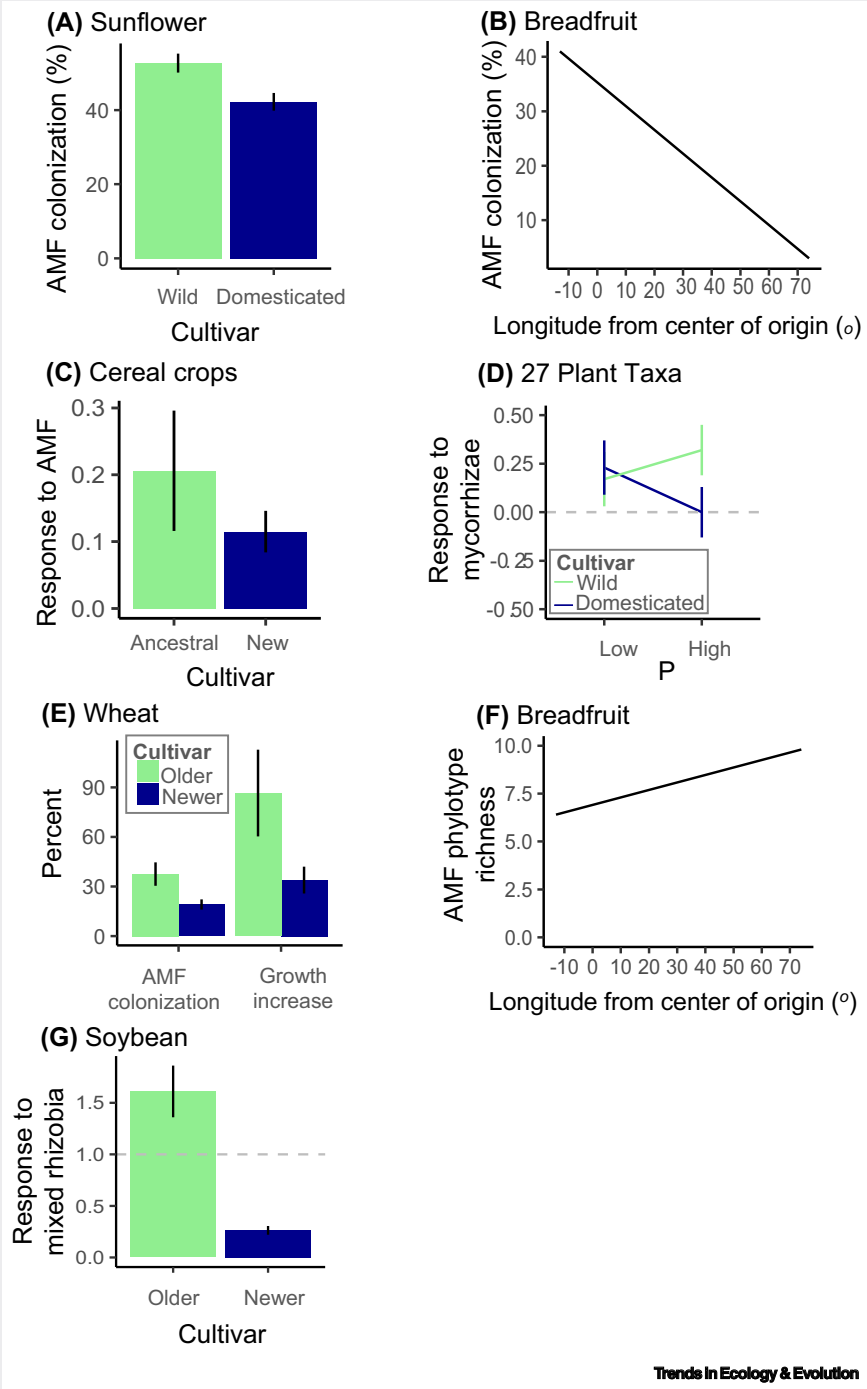

Figure I. Symbiosis Trait Differences among Crop Lineages with Contrasting Domestication Histories. In (G) the broken line at 1.0 indicates the value where benefits to the plant are maximized. Values below 1 indicate plants benefit less from a mix of beneficial and less-beneficial rhizobia than from the beneficial rhizobia alone. Black vertical lines indicate standard error above and below the mean.

Box 3. Evolutionary Ecology of Beneficial Microbes in Agriculture

The impact of domestication on populations of beneficial microbes in agriculture is critical for two frontiers in evolutionary ecology: plant–soil feedbacks and the evolutionary instability of mutualism.

Plant–Soil Feedbacks

Plant–soil feedbacks have a major role in plant health [99]. Plants act as a powerful force to restructure belowground soil microbial communities and, subsequently, microbial community composition has a strong effect on plant performance. Both positive and negative feedbacks on plant health are possible [81]. Negative feedbacks are more common in agriculture than in the wild and are promoted if repeated cultivation of the same crop amplifies crop-specific soil pathogens or suboptimal beneficial microbes [81]. While crop rotation can counteract negative feedbacks, it could have hidden costs if symbionts beneficial to one crop are selected against by rotation crops.

Soil microbiomes amplified by wild versus domesticated crops can be strikingly different [100]. If plants decrease the initiation or maintenance of symbiosis, this can reduce the rewards for cooperative symbionts to the point that they are outcompeted by uncooperative symbionts or become rare. Plants typically allocate resources preferentially toward more cooperative symbionts [101], but if plants do not exert preferential allocation, selection can favor less cooperative symbiont genotypes [63]. If disruption of symbiosis in crops yields symbiont populations with a lower proportion or abundance of cooperative symbionts, this could feedback to reduce selection for symbiosis function in crops.

Plant domestication impacts the evolution of crop microbial symbionts. For crops, such as legumes, that require specific symbiont genotypes to flourish, crop domestication can result in parallel symbiont domestication. As the crop establishes globally, the portion of the symbiont genome that underlies symbiotic compatibility with the host crop is translocated along with the crop because compatible symbionts are required for robust crop growth [102,103].

Evolutionary Instability of Mutualism

Agricultural practices can make resources, such as nutrients, enemy defense, or water, freely available to plants and, correspondingly, the benefits of symbioses that provide these resources to plants are reduced [18,30,33]. If plants subsequently reduce investment in symbiosis, this could lead to the evolution of reduced symbiont cooperation [104,105]. Agricultural conditions could also reduce the density of beneficial microbes so that plant benefit from symbiosis is limited by the low symbiont abundance, which could favor crop genotypes that invest little in symbiosis traits. This could occur if practices such as tilling, crop rotation, or chemical applications to soils [106,107] inhibit symbiosis or reduce symbiont populations [15,66,108].

regulate them, and the evolutionary dynamics of host–microbe interactions, are fundamental goals in evolutionary ecology. As the human population approaches 9.7 billion in 2050, requiring a 1.7-fold increase in crop yields [27,28], the vulnerability of microbial services to degradation makes the achievement of these goals an existential challenge for translational research.

Predictive Evolutionary Models for Symbiosis Traits under Domestication

Distinct evolutionary mechanisms can result in symbiosis trait disruption depending on whether symbiosis traits: (i) trade-off with agricultural traits; (ii) accumulate deleterious mutations due to the demographics of the breeding population; or (iii) are selectively neutral under agricultural conditions. A significant aspect of the evolutionary models we present later, and a key reason to explore this issue more deeply, is that the changes predicted under these models can remain undetected by growers. For instance, reduced interactions between crops and beneficial microbes during domestication can be masked by practices of growing crops in high-nutrient agricultural fields, and could be invisible to breeders who focus primarily on aboveground health.

The Evolutionary Trade-Off Hypothesis

The evolutionary trade-off hypothesis predicts that artificially selected shifts in plant traits, often beyond what was previously shaped by natural selection, can disrupt other plant traits if increases in one trait necessarily result in decreases in another [29]. Physiological constraints can result in a **resource allocation trade-off** between yield and symbiosis. Here, crops evolve reduced symbiosis because the costs of symbiosis compete with allocation to growth and reproduction. Trade-offs can also be driven by **antagonistic pleiotropy**, whereby alleles that are selected under domestication express adverse effects on symbiosis functions. Here, artificial selection

favoring domestication traits outweighs any selection against the reduction in symbiosis that results from these domestication traits. Irrespective of the trade-off mechanism, artificial selection could result in crops that shunt resources to early and large yield traits and sacrifice allocation to symbiosis traits. Thus, adaptation under artificial selection could increase the frequency of alleles that reduce investment in symbiosis (Figure 1).

The devaluation of symbiont services under agriculture that we described earlier can accentuate resource allocation trade-offs between yield and symbiosis. In low-nutrient soils, where many wild crop progenitors thrive, plants benefit from the nutritional services of symbionts [30]. However, symbiotic structures entail costs, and overproducing these structures causes growth deficits [31,32]. Thus, as macronutrients become more available under fertilization, net plant benefit from symbiosis is reduced [18] or can shift toward net cost [33,34]. Under fertilization, plants often downregulate investment into symbiosis [16,17,32] and multiple plant lineages have independently lost the ability to form (or benefit from) symbioses [35–38], suggesting that the costs of symbiosis drive its evolutionary loss and that reduced dependence on symbiosis can be adaptive (e.g., Figure IB in Box 1).

If trade-offs drive canalized declines in symbiosis function, alleles that underlie high performance in agricultural environments (i.e., domestication alleles) are predicted to result in lower symbiosis function. Thus, alleles that confer symbiosis trait disruption could exhibit signals of **positive selection**. For example, alleles that alter phytohormone levels to induce earlier flowering have been favored by artificial selection in crops such as maize (*Zea mays*), but are also predicted to pleiotropically reduce colonization by AMF [39]. Domestication alleles, could be tested for such trade-offs via forward genetics, statistical associations, or quantitative genetics [40,41]. For instance, certain forms of

EVOLUTIONARY HYPOTHESIS	DRIVER	FUNCTIONAL SIGNIFICANCE OF SYMBIOSIS	MODEL OF EVOLUTION	CONDITIONS FOR SYMBIOSIS TRAIT DEGRADATION	GENOMIC OUTCOME
Evolutionary Tradeoffs	Strong selection for agricultural traits that tradeoff with symbiosis traits	Selection on symbiosis traits is overwhelmed by selection on correlated agronomic traits	$\Delta z_1 = \beta_1 V_{A,1} + \beta_2 COV_{A,12}$, (1) [89]	Δz_1, the change in a quantitative symbiosis trait, can be driven indirectly by selection on a correlated trait if the magnitude of indirect selection, $\beta_2 COV_{A,12}$, is greater than that of direct selection on the symbiosis trait, $\beta_1 V_{A,1}$	Alleles that disrupt symbiosis increase in frequency due to artificial selection
Genetic Costs of Domestication	Small effective population sizes and increased inbreeding in agriculture	Selection on symbiosis traits is overwhelmed by stochastic genetic processes	$R = \frac{4N_e s\mu}{1 - e^{-4N_e S}}$, (2) [90]	R, the rate of mildly deleterious substitutions in symbiosis loci, will tend to increase as the effective population size, N_e, decreases	Alleles that disrupt symbiosis accumulate due to stochastic genetic processes such as drift
Selection Relaxation	Lack of selection on symbiosis traits in agriculture	Selection on symbiosis traits is negligible in agriculture	$\nu = \mu$, (3) [92]	ν, the rate of substitutions in symbiosis loci approaches the mutation rate, μ, because these substitutions are neutral	Alleles that disrupt symbiosis accumulate stochastically because selection does not oppose them

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Figure 1. Evolutionary Framework for Symbiosis Trait Disruption in Domesticated Plants: Models of Evolution. Equation 1 shows that evolutionary change in a symbiosis trait, Δz_1, is predicted by the selection gradients acting on the symbiosis trait (β_1), another focal trait (β_2), the additive genetic variance for the symbiosis trait ($V_{A,1}$) and the additive genetic covariance between the symbiosis trait and the focal trait ($COV_{A,12}$) [90]). If $COV_{A,12}$ is negative, sufficiently strong selection for an increase in the focal trait could drive a decrease in the symbiosis trait. Equation 2 shows that the rate of mildly deleterious substitutions in symbiosis loci (R) is predicted by the effective population size (N_e), the strength of selection against such substitutions, (s), and the mutation rate, (μ) [91]. As N_e decreases, R for symbiosis loci will increase, which reflects an increase in genetic drift [92]. Equation 3 shows that the rate of neutral substitutions, (ν), approaches the mutation rate, (μ) [93]. Under relaxed selection, substitutions that disrupt symbiotic function will be neutral traits, and will be fixed at a rate approaching μ for symbiosis loci [92].

pathogen resistance are useful under the novel intense disease pressures imposed on high-density crop monocultures. We predict that modern pathogen resistance alleles may trade off with the maintenance of symbiotic function because plant responses to pathogens and beneficial microbes proceed via similar molecular pathways [42–44], as explored in Box 4.

Box 4. Trade-offs between Plant Immune Defense and Symbiosis

Symbiosis traits can trade off with defense due to the overlap between pathogen defense mechanisms and the regulation of beneficial symbiosis [42,43]. Such trade-offs are distinct from allocation trade-offs, which result if resources allocated to defense leave less to allocate to symbiosis. The genetic basis for some trade-offs between defense and symbiosis are known: the loss of *Reduced Arbuscular Mycorrhization 2* (*RAM2*), a gene that encodes a signaling factor during initiation of plant–fungal infections, not only confers resistance to oomycete pathogens (Figure IA), but also results in the loss of mycorrhization ability [109] (Figure IB). In other cases, negative genetic correlations indicate trade-offs, but the genetic basis for trade-offs remain unknown, such as in the trade-off between legume resistance to pathogenic nematodes and nodulation with nitrogen-fixing rhizobium bacteria [76].

Due to vulnerabilities inherent in symbiosis pathways, immune traits favored by artificial selection could trade off with symbiosis function by excluding beneficial microbiota [5,110]. In a first layer of immunity, plant cells express a conserved set of pattern-recognition receptors (PRRs) that bind to common molecules on pathogenic or mutualistic microbes (microbe-associated molecular patterns, MAMPs) and trigger antimicrobial responses (MAMP-triggered immunity; MTI) [111]. For example, the receptor kinase *CERK1* regulates both fungal pathogen chitin-triggered immunity and arbuscular mycorrhizal symbiosis [112]. Beneficial symbionts have evolved modified MAMPs, inhibited MAMP production, or altered cell-wall composition to avoid plant immune detection [113,114]. Under artificial selection for increased immune function, a sensitized MTI in crops could trigger immune responses against symbionts.

Artificial selection could also sensitize the second, more specialized layer of intra-cellular immunity (effector-triggered immunity, ETI) of the plant, which could result in declines in symbiosis. Under ETI, plants express *R* proteins, nucleotide-binding receptors that detect specific pathogen effectors capable of suppressing MTI [111]. *R* proteins that confer resistance to pathogen effectors could exclude some symbionts because these proteins are also used to restrict the range of symbionts that can successfully proliferate [86,115]. Endophytic fungi [113], rhizobia [116], and mycorrhizae [117] use effectors or lipochitooligosaccharide signals, such as *Nod* or *Myc* factors, which can have ancient pathogenic origins, and enable symbiosis by suppressing the MTI [118]. Finally, soil fertilization can activate defense-related plant genes that inhibit microbial symbiosis [119], as occurs for maize associating with AMF [120] and *Arabidopsis* associating with endophytes [96]. Thus, fertilized soil environments can sensitize plant defenses that decrease plant benefit from symbiosis.

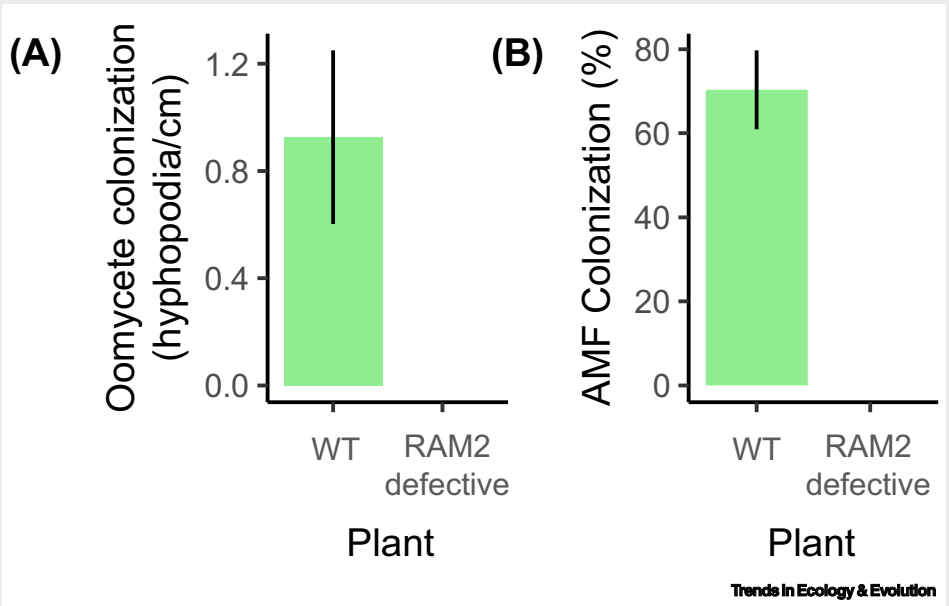

Figure I. Oomycete Resistance due to Loss of *Reduced Arbuscular Mycorrhization 2* (*RAM2*) Results in Loss of Mycorrhization Ability compared with Wild-Type (WT) [109].

Plants could adapt to avoid some of the trade-offs we describe. Plants could evolve more sensitive adaptive plasticity [17] to express robust symbiosis traits if symbiotic resources are in short supply and to reduce investment in symbiosis if the rewards of symbiosis are freely available in the environment (see Outstanding Questions). For example, in the model symbiosis between legumes and rhizobia, plants adjust root nodule formation and nitrogen fixation. In autoregulation of nodulation, rhizobial infection activates the transcriptional regulator, NIN, triggering systemic long-range signaling between roots and shoots to inhibit further nodule formation [17,32]. Furthermore, high soil nitrate levels activate a related NIN-Like Protein, NLP, which triggers the same long-range signaling to inhibit nodule formation and nitrogen fixation [17,32]. Plant species differ with respect to the plasticity of symbiosis traits. Negative genetic correlations between the ability to benefit from symbiosis in low-resource environments and the ability to divest from symbiosis under high-resource conditions could hinder the evolution of adaptively plastic symbiosis in crops, but this remains to be tested.

The Genetic Costs of Domestication Hypothesis

The small effective population sizes and low diversity of domesticated plant populations can result in stochastic increases in the number and frequency of deleterious genetic variants [45]. Deleterious genetic variants can accumulate stochastically, despite selection against them (Figure 1) if: (i) the small effective population sizes common in domesticated plants reduce the efficacy of selection relative to **genetic drift**, allowing for fixation of mildly deleterious mutations [45–47]; (ii) strong artificial selection results in '**genetic draft**', whereby deleterious mutations hitchhike to high frequency because they are linked to genes that fix under strong artificial selection [45,48,49]; (iii) domesticated plants experience '**expansion load**', wherein deleterious mutations reach high frequencies via drift after a demographic bottleneck [50]; (iv) inbreeding during domestication decreases the efficacy of **recombination** in breaking up linkage between beneficial and deleterious loci [51], reducing the chance of beneficial alleles moving into a genomic background with fewer linked deleterious alleles [52,53].

Disruption of symbiosis functions in crops can occur as a demographic consequence of domestication, despite selection against deleterious variants at symbiosis loci. While deleterious alleles are more common in crops than in their wild relatives [46,47,50,51,54], we lack tests of genetic costs for symbiosis traits. Research has begun to annotate and map symbiosis loci in plant genomes (e.g., [55,56]), yet the impact of genetic costs on symbiosis function remain unknown. **Linkage disequilibrium** (LD) tends to be more extensive in crops than in their wild relatives [51]. Higher LD in inbred crops reduces the probability that deleterious symbiosis alleles are purged when linked to beneficial alleles and increases the probability that beneficial symbiosis alleles linked to strongly deleterious alleles will be lost [51]. We predict that deleterious symbiosis alleles will be enriched near loci of agronomic importance that have been subject to selective sweeps, and in regions of low effective recombination rate [45,46], as occurs for deleterious variants in soybean and sunflower (*Helianthus annuus*) [46,50], although there is mixed evidence for maize [53,57]. If some deleterious symbiosis alleles have hitchhiked with a linked beneficial allele, as occurs for one in ten deleterious alleles in maize [53], these deleterious symbiosis alleles will exhibit signals of positive selection [58].

The impacts of deleterious alleles can be substantial [46,50,51]. For example, a deleterious allele linked to artificially selected semidwarfed stature in rice resulted in severe drought sensitivity in modern dwarfed rice cultivars [49]. Structural variants, such as deletions, insertions, duplications, inversions, and translocations, have a critical role in domestication evolution, yet their impacts on symbiotic function in crops are unexplored [45,59]. The extent to which the stochastic forces we highlight disrupt symbiosis traits remains a frontier in plant science. Since these forces are

stronger in populations with smaller effective population sizes, their negative impacts on symbiosis function are likely exacerbated in crops compared with wild crop relatives.

The Selection Relaxation Hypothesis

The Selection Relaxation Hypothesis predicts that some traits critical for plant fitness in the wild experience relaxed selection in agriculture. Traits that do not contribute to success in agriculture will stocastically accumulate deleterious genetic variants because these mutations are not removed by artificial selection [50,52,60]. In contrast to genetic costs, relaxed selection results when artificial selection on a trait is weaker than natural selection in the wild, irrespective of demography. As neutral traits, alleles that disrupt symbiotic function will accumulate at a rate approaching the mutation rate because artificial selection no longer purges them, and they increase in frequency via drift and hitchhiking [61] (Figure 1).

Selection relaxation can be tested experimentally. Under selection relaxation, robust symbiosis traits confer no fitness advantage over disrupted symbiosis traits in agricultural conditions, yet robust symbiosis traits are advantageous under less luxuriant conditions. This predicts indistinguishable genotypic selection gradients for symbiosis traits among plant genotypes that differ in symbiotic function under agricultural conditions, but are under selection to maintain robust symbiosis traits elsewhere [62–64]. If artificial selection is relaxed on symbiosis traits, but remains strong on other traits in domesticated plants, we predict that domesticated, but not wild progenitor, plants will exhibit an elevated **ratio of nonsynonymous to synonymous substitutions** in symbiosis genes, and that nonsynonymous substitutions will reach higher frequencies and induce more radical amino acid changes to symbiosis loci, than in other functional regions of the genome.

The selection relaxation hypothesis predicts that a lack of artificial selection on symbiosis traits in the fertile, high-nutrient, low-stress environment of agriculture results in the disruption of symbiosis function in crops. Consistent with this hypothesis, diverse crop taxa have evolved a reduced ability to associate with mycorrhizae under high levels of phosphorus fertilization, which is assumed to relax selection on phosphorous uptake [8,13]. Agricultural soils can harbor low densities of microbial symbionts due to the disruptive impacts of tillage, rotational planting, chemical inputs, or crop rotation patterns [6,15,65–67], which could further relax selection on symbiosis traits in plants (Box 3). These examples are consistent with, but do not directly test, the selection relaxation hypothesis. Traits that no longer confer a benefit under intensive agriculture could include the ability to preferentially acquire nutrients from superior symbionts (e.g., via partner choice or sanctions) because resources may be freely available from fertilizers, or the ability to enhance defense from antagonists based on microbial symbiosis, because pesticides may reduce selection due to these pests. The selection relaxation hypothesis predicts that germplasm bred under more intensive agricultural conditions will exhibit greater symbiosis trait disruption than germplasm bred under less intensively managed conditions. We note that not all traits decay under relaxed selection: symbiosis traits might not decay during domestication if new or secondary functions result in high yield, if symbiosis traits are positively genetically correlated with traits that result in high yield, or if crops retain gene flow with wild populations where the trait is under selection for function [60,68].

Maximizing the Benefits of Symbiosis in Crops

Identifying pathways of symbiosis disruption will inform strategies to maximize the benefits of symbiosis in crops. Under the genetic costs and relaxed selection hypotheses, symbiosis traits are degraded stochastically and there is potential to increase yield or symbiotic function by the **introgression** of desirable symbiosis loci from wild or related lineages into crops [69,70], similar to the introgression of desirable disease resistance loci from wild congeners into crops [71]. Genomic regions with fewer deleterious variants have introgressed into maize from wild populations

[70], and resistance to a fungal pathogen in wheat appears to result from introgression with wild populations [72]. Symbiosis function could be improved in a similar manner. **Hybrid production** of seed by crossing distinct breeding pools could allow complementation of deleterious variants if different breeding pools have deleterious alleles at different loci [51]. In soybean and barley (*Hordeum vulgare*), ~40% of deleterious variants are private to individual cultivars and could be purged from breeding populations [46]. In regions with low effective recombination, it is difficult for breeding programs to purge deleterious alleles, so targeted introgression, hybridization, and gene editing could be useful in these regions [73,74]. These approaches could precipitate the development of more symbiotically robust crop cultivars better able to thrive under less resource-intensive methods of sustainable agriculture [75].

Symbiosis traits that degrade because of trade-offs are more difficult to overcome because they suggest that the genetic variants most strongly favored in modern agriculture are in conflict with robust symbiosis. Characterizing trade-offs between symbiosis traits and agriculturally significant traits requires measuring yield traits and symbiosis traits under selection and finding negative trait covariances. The genetic basis for these trade-offs can reflect either fundamental biophysical constraints, or genetic linkage between loci under opposing selection regimes [76]. Evolutionary trade-offs due to fundamental constraints are difficult to overcome because possible paths to minimize trade-offs across the adaptive landscape have likely been unsuccessfully tested by selection over evolutionary time [77]. Due to these constraints, variants that increase plant investment in symbiosis will be detrimental to overall agricultural performance. However, trade-offs that are driven by genetic linkage can be alleviated by breeding programs that select for recombination events that break up such linkage. Trade-offs can also be alleviated by gene duplication, or by tissue-specific or ontogenetic stage-specific gene regulation [76]. Finally, trade-offs between yield and symbiosis function could be accentuated only under specific agricultural conditions; under altered conditions, such trade-offs might be reduced.

The three genetic scenarios we highlight would motivate contrasting crop breeding strategies. Under relaxed selection and genetic costs models, symbiosis traits are disrupted stochastically (i.e., for no good reason), so restoring these traits to all varietal backgrounds would be beneficial. However, under the trade-off model, there would be costs to restoring symbiosis traits to elite varieties designed to perform in high input conditions, while there could be strong benefits for varieties grown in low input conditions. Given these dependent effects, targeted breeding programs for distinct high versus low input agricultural conditions would be beneficial.

Concluding Remarks

Efforts to maximize symbiosis benefits in crop plants have focused on the characteristics of microbial strains and consortia within symbiotic inocula [24,25,78,79]. However, optimizing the symbiosis traits of the crop plants themselves should have a bigger impact on improving symbiotic benefits in agriculture [6,80]. To understand the plant symbiosis traits that evolved during domestication, we must understand how trade-offs, relaxed selection, and genetic costs in domesticated plants impact symbiotic regulation. This will be key to success in increasing the benefits of microbial symbiosis in crop germplasm [6,81] and designing synthetic symbioses that hold great promise in modern agriculture. For example, understanding trade-offs incurred by symbiosis traits and any ways in which symbiosis traits are more robust in the wild relatives of crops could aid breeders in minimizing the costs of symbiosis in current efforts to develop a novel capacity for symbiotic nitrogen fixation in nonleguminous crops, such as maize [82,83]. Research on symbiosis trait disruption in crops will also serve as a model system for understanding fundamental patterns and mechanisms of the evolution of reduced investment in microbial symbiosis by host organisms, which appears to be a common evolutionary pathway (see Outstanding Questions).

Outstanding Questions

Are differences in symbiosis traits between crops and wild relatives adaptive, deleterious, or neutral? Understanding symbiosis traits and their shifts under artificial selection is critical to breeding efforts that target symbiosis function.

Are there trade-offs between symbiosis benefit and dependence? If no trade-off exists, it might be possible to breed for crops that can not only benefit strongly from symbiosis, but also perform well if key symbionts are lacking.

What are the genomic bases of symbiosis function? Addressing this outstanding question would enable researchers to examine the plant molecular mechanisms that have been recruited for symbiosis, including pathogen defense, developmental pathways and/or organogenesis, and nutrient cycling. Researchers can test for molecular signatures predicted by the three frameworks detailed in the main text by focusing on sequence evolution, gene presence, regulatory sequences, coding regions, or gene expression. Genome scans can reveal whether regions exhibiting signatures of drift or selection include symbiosis loci. These analyses are limited by the quality of annotations of genomic regions that impact the symbiosis traits of plants.

Which symbiosis traits are associated with fitness benefits or plant performance? Research typically evaluates microbial impacts on overall yield, with less focus on identifying genetic, physiological, and morphological mechanisms that underlie plant benefit from symbiosis, yet these mechanisms will be key for future breeding efforts.

What is the composition of the microbiome associated with crops versus their wild relatives and what are the consequences of any differences in the microbiome for plant performance across contrasting environments? Investigating these questions will help to broaden our understanding of the diversity of microbial symbionts that differentially impact crops and their wild relatives and could provide tools for developing useful inocula.

A more complete characterization of symbiosis function in crops is needed to inform diverse aspects of agriculture (see Outstanding Questions). Few modifications to genetically engineered crops are tested for impacts on symbiosis, yet alterations of immune function [84] or phytohormone production [39] can impact symbiosis with beneficial microbes. It is critical to understand whether key symbiosis traits trade off with disease resistance, or whether variants with deleterious symbiotic effects are fixed in crops, to successfully design a robust symbiosis [4], potentially via genome editing [73]. Other agricultural practices, such as grafting perennial crops onto the rootstock of wild relatives to confer resistance to pathogens and abiotic stress [85], are rarely assessed for their impact on symbiosis. New studies should analyze whether more robust symbiosis could contribute to the benefits of such practices.

Alleles or genotypes that improve symbiosis outcomes for crops should be targeted via marker-assisted breeding programs. One goal would be to develop generalist cultivars, able to benefit from symbiosis with indigenous microbes in diverse locations [24,86]. Nodule cysteine-rich peptides, which modulate plant benefits from rhizobia, could be fruitful targets for engineering legume–rhizobia partnerships with improved agricultural properties [87]. Moreover, feral crop populations [88] could harbor superior symbiosis alleles with low negative epistatic effects in the genomes of crops due to their close relatedness. Selection for symbiosis function might be stronger on feral crops than on crops in modern agriculture, but these populations can face similar genetic costs to domestication, such as reduced genetic diversity relative to wild progenitor species. In addition, weeds are unintentionally domesticated plants: studying whether weeds experience symbiosis trait disruption could compliment work in crops because, while weeds adapt to the same agricultural conditions as crops, they are not subject to the same targets of artificial selection.

Understanding how trade-offs, genetic costs, or relaxed selection impact symbiosis will inform efforts to engineer crops with novel symbiotic capabilities [83]. Microbial symbionts provide foundational services to agricultural crops. Rhizobia alone fix 70 million metric tons of N annually [89], valued at US $23–$59 billion worth of fertilizer application [30]. Resolving the impact of domestication processes on symbiosis function in crops, and maximizing the benefits of symbiotic function in elite cultivars, has the potential to have a pivotal role in meeting the challenges to food security we face in the coming century.

Author Contributions

S.S.P. and J.L.S. collaborated on the ideas and writing in the manuscript.

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