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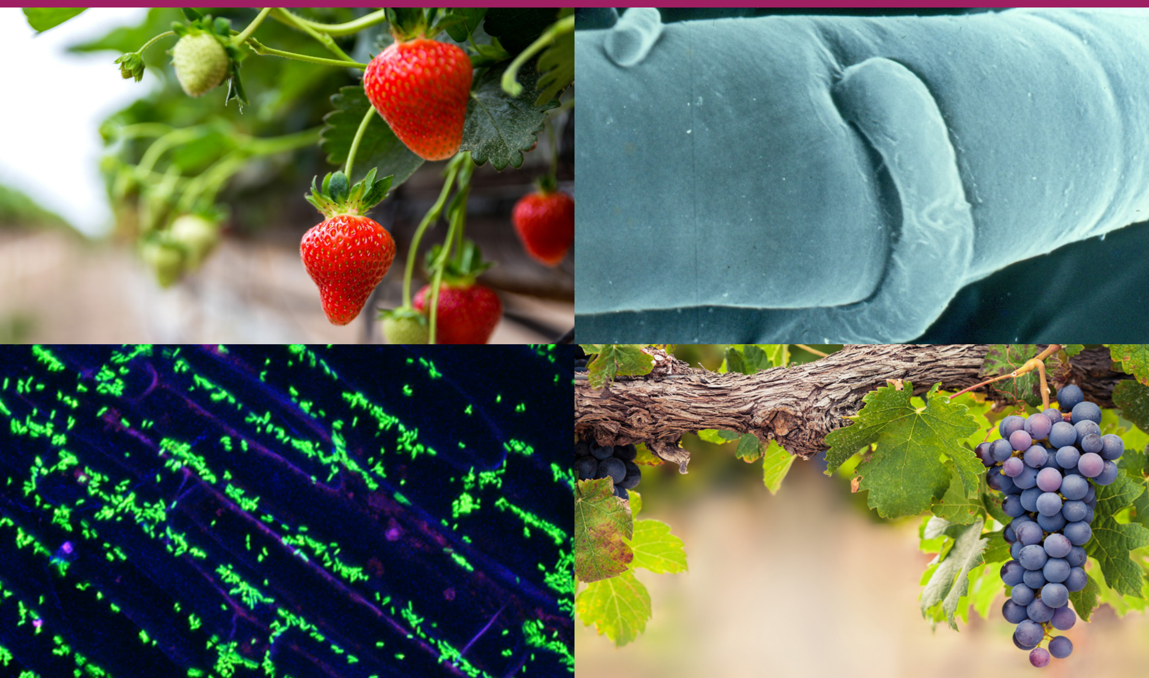

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1 Introduction

1.1 Developments in the past

The role of bioprotectants in agriculture depends on the crop protection approaches applied in cropping systems. Approaches towards crop protection have changed during the last few decades and will continue to change. Changes in crop protection approaches allow changes in cropping systems and vice versa, and are driven by economic and societal conditions and needs as well as by the available crop protection technologies and the development of new ones. Major technological developments have determined disease control approaches during the last few decades. New breeding technologies have increased the level of resistance against pathogens in certain crops and the development and broad implementation of chemical crop protection have reduced yield losses through disease in nearly all crops (Oerke et al., 1994). Saving yields by the broad application of chemical crop protection have allowed farmers to simplify their cropping systems (Barzman et al., 2015).

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Measures for disease prevention, such as the use of resistant varieties, crop rotation and high biodiversity at field and landscape level, have become less important. Cropping systems developed in large-scale production, simplified crop rotation or monocultures and the use of cultivars more susceptible to diseases gave higher yields in combination with chemical crop protection. Consequently, cropping systems became less resilient against losses caused by diseases and more dependent on the use of chemical crop protection.

The main drivers encouraging a change in crop protection approaches during the last few decades have been drastically increased by demand for food, feed and fibre for a growing world population, in combination with a shift in nutritional patterns of consumers towards animal protein food. The latter has resulted in a disproportional increase in feed production. An increasing awareness of the shortcomings of green revolution technologies has resulted in the adaptation of agricultural production systems, often guided by government regulations and demanded by consumer perceptions. Retailers even increased the pressure on levels of pesticide residues in food by setting more restrictive standards than legally enforced for residue levels. This has led to restricted use of chemical pesticides in advanced integrated pest management (IPM) systems (Barzman et al., 2015).

1.2 Drivers of change

Current major technological progress will further shape crop protection approaches. Better epidemiological knowledge results in reliable forecasting of certain disease epidemics, particularly concerning risk periods for infections by pathogens. This knowledge is implemented in decision support systems (DSS), guiding farmers on decisions regarding chemical crop protection, especially on the timing of applications. Developments in precision agriculture allow site-specific applications of crop protection products within fields and advanced spraying technologies allow targeting of relevant plant parts with reduced drift to the environment. This may result in reduced use of crop protection products per hectare, which results in reduced unwanted environmental side effects.

Reduced efficacies due to resistance development by pathogens against fungicides, and restrictions in the use of chemical crop protection (and subsequent withdrawal from the market) in combination with further requirements, such as those of the European Parliament (2009) to change cropping systems towards systems with IPM, is currently causing another shift towards more resilient cropping systems. In such systems, the implementation of preventative measures is preferred in combination with chemical crop protection as a last resort if other measures do not sufficiently safeguard crop yields (Barzman et al., 2015; Baker et al., 2020). This will result in the development of new complex and multi-faceted IPM systems.

1.3 Future developments

Future developments in crop protection approaches are difficult to predict. Systems may slowly develop in incremental steps towards complex IPM systems with strongly guided application of crop protection products. However, the consequences of climate change and the current pressure on the environment (resulting in the degradation of soils, pollution of waterways and ground water and a decrease in biodiversity in agricultural systems and their surrounding wildlife habitats) are leading us to re-think the direction and speed of changes needed in the near future. Societal awareness of planetary boundaries and the impact of humans on ecosystems (including but not limited to climate change during the Anthropocene) may force much more rapid and drastic changes in significant transformational rather than slow incremental steps (Steffen et al., 2015). This will encourage the development of drastically changed cropping systems with closed nutrient cycles, restricted use of external resources and full protection of biodiversity (Dainese et al., 2019; van Selm et al., 2020; Willett et al., 2019; van Zanten et al., 2019). Yield may decrease per hectare compared to current high-input systems that depend on the external use of fertilizers, energy and crop protection products. Yield gaps of 8–25% have been reported by a complete switch to organic farming (Muller et al., 2017). To feed the population, the need for food production on the limited available arable land will not allow significant competing feed production for livestock industries. Such changes are only possible in combination with diet changes from animal protein to plant protein nutrition. There will be a need to produce protein food crops to fulfil future nutritional patterns instead of abundant cereal production and fodder maize for animal feed (van Selm et al., 2020; van Zanten et al., 2019). Such transformational changes in cropping systems will result in higher diversification in crops at temporal and spatial scales, a shift to other/new crops, and will have a strong emphasis on the resilience of cropping systems against the negative impacts by pests and diseases (Beillouin et al., 2019). In this context, an understanding of the use of microbiomes of soil, in and on plants and in crop residues, will be of increasing importance to maximize the impact of microbiomes on resilience and plant health (Bakker et al., 2020; Berg et al., 2020; CAST, 2020; Kerdraon et al., 2019; Syed Ab Rahman et al., 2018). Crop residue management will become an important preventative measure to reduce pathogen populations (Köhl et al., 2007). Advances in assessing microbiome components and functions are expected during the next few years so that biological information can be incorporated into the next generation of precision and digital agriculture technologies and effective microbiome transplant methods for field use will become available.

1.4 The role of bioprotectants in cropping systems

It is obvious that bioprotectants contribute in various ways towards the different crop protection approaches, ranging from the frequently used reliance on routine use of chemical crop protection products towards a possible future system relying strongly on the resilience of the cropping system with restricted use of chemical crop protection products. Currently, bioprotectants mainly complement and/or replace chemical crop protection products in spray schedules. In the envisaged future, bioprotectants will complement the functions of the microbiome and other components in the cropping system contributing to resilience against plant diseases. Multiple-strain biological control products may be designed for this purpose (Niu et al., 2020). Targeted diseases will change with changing crops and cropping systems, as well as the demands on the specificity of bioprotectants to guarantee protection of the beneficial microbiome. Consequently, different bioprotectants are needed now and in the future.

The process of development of bioprotectants – from choosing the targeted pathogens to screening candidate antagonists, product development, registration and market introduction – takes many years; often 10–15 years are needed for their broad implementation in agriculture. This chapter aims to give a brief overview of the particular roles of bioprotectants in current and potential future crop protection approaches to stimulate discussion within the biocontrol industry, amongst scientists and funding agencies on the need for new generations of bioprotectants for an agricultural industry undergoing transition.

2 The role of bioprotectants in conventional high-input cropping systems

In conventional cropping systems, high inputs of crop protection products are used to achieve maximum yields. Fungicides are intensively applied to prevent or control pathogens damaging the crop. Driving forces for crop protection measures include the avoidance of risks of losses, the expected efficacy of a measure and product and application costs. Broad-spectrum fungicides and combinations or alternations of different crop protection products are standard.

A first prerequisite for the integration of bioprotectants into such crop protection approaches is their biological compatibility. Living microorganisms as the active ingredients of bioprotectants may not survive or at least be restricted in their activity in an environment where multiple applications of different fungicides, including broad-spectrum products, are used. A possible solution is the selection of biological control strains that are resistant to one or several frequently used fungicides. However, fungicides used by growers will change

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over time due to changes in availability on the market and the occurrence of new compounds and mixtures of active ingredients. It will be impossible to respond to this development rapidly with the development of bioprotectants with adapted resistance to newly introduced fungicides. If bioprotectants compatible with synthetic fungicides are available and can be integrated into crop protection spray schedules, growers will compare the advantages of applying chemical fungicides versus bioprotectants. Product costs will be considered, notwithstanding the externalized costs (Pimentel and Burgess, 2014a,b; Bourguet and Guillemaud, 2016), ease of application in tank mixes including other pesticides or fertilizers, spectrum of activity from high specificity to control one disease to a broad spectrum including several diseases and direct efficacy in disease control with a rapid effect on symptom development without considering indirect, long-term effects through saving the resilience of the cropping system. Based on such considerations, the grower may decide in many cases to use synthetic fungicides instead of bioprotectants, as long as fungicides are available without any restrictions in use. Only if efficient synthetic crop protection products are not available growers will use bioprotectants as an alternative. An example is the use of bioprotectants for fire blight control in apple and pear production if the use of antibiotics such as streptomycin or copper products is restricted. The use of certain fungicides can also be restricted because of the risk of resistance development by the targeted pathogen. If no efficient fungicides are available to replace the preferred fungicides with restricted use, bioprotectants can be integrated into the spray schedule to reduce the risk of fungicide resistance development in the pathogen population. However, the most important motivation for conventional growers to integrate bioprotectants into their spray schedules may be restrictions in pesticide residue levels set by government regulations, such as the 'Maximum Residue Level' (MRL), or (often at lower levels and with further restrictions for multiple pesticide residues) by retailers (Buurma et al., 2012). Late season applications of bioprotectants that don't leave residues on the marketable product have a competitive advantage over synthetic fungicides to avoid higher residue levels of a certain fungicide or to obtain a product with a lower number of different fungicide residues.

In conclusion, there are limited niches for bioprotectants in conventional crop protection approaches where only short-term costs and benefits are valued but externalized costs and long-term benefits are not considered.

3 The role of bioprotectants in integrated pest management cropping systems

3.1 The principles of integrated pest management

Integrated pest management (IPM) is an essential component of current sustainable farm management. By avoiding routine applications of chemical pesticides, contamination of ecosystems and undesirable effects on human and animal health are reduced. In IPM, complex crop protection strategies are being developed and are applied to build on resilient crops, complex ecosystems with high buffering capacity against populations of plant pathogens and pests, and a preference for environmentally friendly crop protection products before chemical pesticides are applied as an exceptional intervention (Barzman et al., 2015).

Entomologists realised in the 1950s that broad-spectrum insecticides favoured pest outbreaks since natural enemies had been eliminated. IPM is a response to the experienced development of pesticides resistance and damage of beneficial insect populations. Important components of IPM include multiple tactics to monitor and develop and use action thresholds to keep populations under predetermined damage levels (Baker et al., 2020). Protection and enhancement of populations of natural enemies in combination with applications of selective insecticides only after pest thresholds are reached are the pillars of IPM. The original goals of IPM were to reduce dependency on pesticides and to protect the environment and health in combination with avoiding rapid resistance build-up against the pesticides by the targeted pests. Later, cultural tactics from mulch covers to tillage were added, combined with biological and chemical control (Baker et al., 2020).

Current IPM approaches cover whole crop protection, preventing damage by pests, diseases and weeds. IPM has developed a broad application in agriculture. In the European Union (EU), Directive 2009/128/EC (European Parliament, 2009) promotes the use of IPM through the development and implementation of National Action Plans in Member States since 2014, with the emphasis on growing healthy crops with the least possible disruption to agro-ecosystems and encouraging natural pest control mechanisms. The system approach is structured by eight principles (Barzman et al., 2015). Prevention and suppression of harmful organisms is always the basic first principle, for example, combining crop rotation, cultivar choice, cultivation techniques, avoiding the spread of harmful organisms and engagement of beneficial organisms, including protection of an ecological infrastructure outside production sites. Decisions regarding direct responsive crop protection measures are made only if monitoring of the crop and its pest populations and diagnostics indicate the relevant risk of crop damage by a harmful organism. Sustainable biological, physical and other non-chemical methods must be used before synthetic pesticides, if they provide satisfactory pest control (see Fig. 1; Annex III of Framework Directive 2009/128/EC; Barzman et al., 2015).

The IPM approach strengthens the position of biological control compared to conventional cropping systems where the use of bioprotectants is mainly motivated to reduce residue levels in food and feed products and to avoid the build-up of resistance to synthetic fungicides. In IPM, preferred measures

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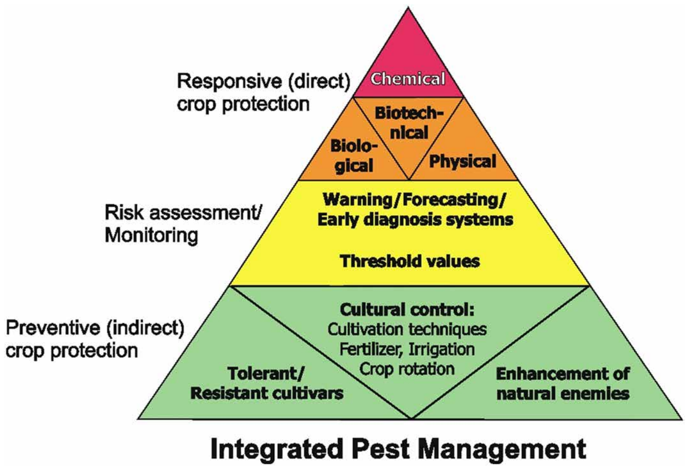

Figure 1 The principles of IPM (Meissle et al., 2011; modified by Meissle).

for preventative crop protection protect or even enhance naturally occurring biological control by natural enemies of pests and beneficial components of the microbiomes in soil, in and on plants and their residues. Resilience in the cropping system increases due to natural biological control, so that less synthetic crop protection products have to be applied and, if applied, selective products with limited negative impact on the natural biological control should be chosen in IPM. In modern IPM systems, including the framework described in the directive on sustainable use of pesticides in the EU (European Parliament, 2009), sustainable biological, physical and other non-chemical methods must be given priority over chemical methods if they provide 'satisfactory' pest control. The definition of 'biological methods' in this context is often broad and may include pheromones, plant extracts, culture extracts of microorganisms or purified metabolites of microorganisms or plants, although the scientific definition of biological control of plant diseases is the suppression of populations of plant pathogens by living organisms (Heimpel and Mills, 2017; Stenberg et al., 2021). In current IPM, the preferred selective control methods are those that are not harmful to the resilience of a cropping system before broad-spectrum methods are used that likely cause side effects on components of the natural biological control of the system. Consequently, following this way of thinking, it is important also to distinguish between selective and broad-spectrum methods in biological control. Zehnder et al. (2007) introduced such a separation for arthropod pest management. They proposed, after preventative strategies have been considered, the inundative and inoculative release of biological control agents as the first phase of a control strategy. In this phase of pest control, mass-reared live agents are released (Eilenberg et al., 2001). Only if control levels of selective biological control agents are insufficient, insecticides of biological and mineral origin and further compounds such as pheromones for mating disruption are applied in the next phase of pest management strategy (Zehnder et al., 2007). Niggli (2020) modified the pest management strategies proposed by Zehnder et al. (2007) by including disease management strategies. In the early phases of preventative measures, he included vegetation management to enhance soil microbiome inducing resistance in plants. In the next phases of disease control measures, the release of competitive antagonists against diseases is proposed, followed by the use of fungicides of biological and mineral origin and the use of chemical or synthetic fungicides (including copper) in the final phase.

3.2 Bioprotectants in integrated pest management

Compared to conventional cropping systems, the IPM approach strengthens the position of bioprotectants. The use is not complementary to the use of chemical pesticides as in conventional cropping systems, but rather biological control products with satisfactory potential in disease protection have to be used before chemicals are considered. In the EU, this principle is strongly promoted and should be implemented by the Member States (European Parliament, 2009). For the broader implementation of bioprotectants in IPM, the decision-making process for growers needs to be adapted. The use of protective measures depends on a decision-making process, often supported by sophisticated DSS developed by commercial providers. Such systems advise farmers in the timing of application of synthetic fungicides. Since the modes of action of bioprotectants are very different from those of synthetic fungicides, optimum timing of bioprotectant application may differ from the advised timing of fungicide applications. Bioprotectants may work more slowly, may need to be applied earlier during epidemics or even before a crop is established (as is the case in controlling disease outbreaks of *Sclerotinia sclerotiorum* by destroying overwintering sclerotia of the pathogen by applying hyperparasites on and in the soil (Gerlagh et al., 1999; Zeng et al., 2012)).

There is therefore the need to develop adapted DSS considering the modes of action of bioprotectants. There is also a need to evolve such DSS from the view of short-term disease to a decision-making process including systemic factors in a long-term decision strategy (Barzman et al., 2015). A change of mind is also needed regarding the understanding of the satisfactory potential in disease protection. This cannot simply consist of a comparison of the efficacy of bioprotectants and synthetic fungicides in experimental design as conventionally used for efficacy tests for crop protection products. Bioprotectants may work more slowly, and have to be applied based on different decisions as conventional fungicides because they work not only by a direct effect of the applied organism but also by the support and protection

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of the buffering resident microbiome, whereas fungicides may affect beneficial non-target organisms. Furthermore, due to their pathogen-specific nature, it is unlikely that the application of bioprotectants will result in new disease problems, which is often the case when broad-spectrum fungicides are used with side effects on beneficial non-target organisms. In this situation, fungicide use may encourage the additional use of other complementary fungicides to control such new disease problems (Barzman et al., 2015). As long as such possible effects (as well as other externalities causing costs for the society) are not considered in the decision-making process, fungicides may be preferred due to their faster and stronger direct control activity (Pimentel and Burgess, 2014a,b; Bourguet and Guillemaud, 2016). The strong position of bioprotectants in IPM approaches will thus become reality after a broad and long-term holistic definition of the satisfactory pest control level has been developed and applied.

4 The role of bioprotectants in organic cropping systems

4.1 Disease prevention

Organic agriculture relies on ecological processes, biodiversity and closed nutrient cycles rather than external inputs with adverse effects (http://www.ifoam.org/about_ifoam/standards/index.html). The underlying principles of organic agriculture are described by the International Federation of Organic Agricultural Movement (IFOAM) in Best Practice Guidelines and detailed organic standards and technical regulations. Governmental regulations, such as in the EU (European Commission, 2007) and the United States (United States Dept. Agric., 2011), regulate production in organic agriculture and the marketing of organic products. A worldwide certification system for organic farms and their products guarantees that organic agriculture follows the principles of the organic movement. This includes the entire chain, from organic seed production to retail.

The essential principles of organic crop production are biological cycles within the farm, closed systems regarding nutrients and organic matter, maintenance of high genetic diversity and avoidance of any form of pollution (Van Bruggen and Finckh, 2016). Farming systems should be self-regulating through interdependent natural processes in the agroecosystems with the emphasis on prevention of problems rather than solutions by use of external inputs. Typical elements in organic cropping systems are higher plant diversity in time and space due to complex rotation systems, smaller field plots, mixed crops and acceptance of certain weed levels in the crops. Soil management (including the cycling of organic matter within the farm) leads to higher organic matter in the soil and consequently higher microbial colonization levels and higher microbial diversity in the soil, as well as on above-ground parts of the crops and their residues. Organic cropping systems clearly differ from conventional cropping systems. The intrinsic properties of organic systems strongly determine the occurrence and intensity of plant diseases (Van Bruggen and Finckh, 2016), which results in disease management challenges different to those in conventional cropping systems. Consequently, the role of bioprotectants in plant disease control in organic cropping systems differs from their role in conventional cropping systems.

The importance of plant diseases in organic and in conventional cropping systems has been extensively reviewed by Van Bruggen and Finckh (2016), who analysed scientific reports on root and foot diseases in monocotyledonous and dicotyledonous arable crops, annual vegetable crops and perennial crops. Such diseases are caused by soilborne pathogens that interact with the saprophytic microorganisms active in soils. Healthy soils with sufficient organic matter and high biodiversity strongly influence populations of soilborne pathogens and thus generally lower the risk of foot and root diseases. These diseases are generally less pronounced in organic systems compared to conventional cropping systems. For foliar diseases, differences between cropping systems are harder to evaluate because airborne inocula of diseases may be transported for longer distances and thus neighbouring effects may mask system effects (Van Bruggen and Finckh, 2016). A general observation is that certain foliar diseases such as rusts and powdery mildews are favoured on plants grown at high nitrogen levels. Since nitrogen levels are generally lower in organic cropping systems, such diseases affect organic crops less severely than conventional crops. For the prevention of foliar diseases, different measures are combined in organic farming. Examples are sanitation by removal of inoculum sources, cultivar selection with an emphasis on general robustness against biotic stresses and increased habitat diversity, including use of strip crops, intercropping, mixed crops and cover crops (Ditzler et al., 2021). Van Bruggen and Finckh (2016) identified in their study the multicyclic foliar pathogens causing problems for organic growers where preventative measures are often not satisfactory and disease control measures have to be applied. Examples of such threatening diseases are late blight in potato, downy mildews in many crops and apple scab. For many other foliar diseases, differences between the cropping systems were less pronounced or diseases were less severe in organic cropping systems compared to conventional systems.

4.2 Use of crop protection products

The use of plant protection products in organic agriculture has to be authorized by general governmental regulations for plant protection products. Besides this, an additional approval for use in organic agriculture is needed (European Commission, 2008; Speiser and Tamm, 2011). Plant protection products approved for use in organic agriculture are 'mined natural products' such as copper, sulphur and silicates, salts such as bicarbonate salts, oils, extracts from plants and microorganisms, and microorganisms (European Commission, 2008; Van Bruggen et al., 2016). The use of living microorganisms (bacteria, viruses and fungi) for pest and disease control is generally allowed in organic agriculture as long as microorganisms are not genetically modified and no petroleum-based synergists or carriers are used in their formulation (Speiser and Tamm, 2021; Van Bruggen and Finckh, 2016).

Currently, copper fungicides are widely applied in organic farming to control major multicyclic diseases in organic farming such as late blight in potato, downy mildew in grapevine and apple scab (Lamichhane et al., 2018). The use of copper fungicides in the EU is restricted by regulations, allowing only gradually decreasing amounts applied per hectare due to the unwanted accumulation of copper in the soil and negative effects on soil biota. It can also be expected that broad-spectrum copper fungicides interfere with phyllosphere microbiomes so the natural microbial buffering capacity against foliar diseases might be affected. However, studies on the effect of multiple copper applications in grapevine revealed no differences in fungal microbiome composition and quantitative levels of fungal populations on grapevine leaves during a growing season (Gobbi et al., 2020). For other broad-spectrum fungicides such as lime sulphur and sulphur used in organic farming, negative effects on beneficial microorganisms can be expected but conclusive results of microbiome studies on such side effects are missing. As long as broad-spectrum fungicides are commonly used in organic farming to control the major leaf diseases, the role of bioprotectants will be limited. However, similar to the development of IPM, use of selective crop protection products should be considered before broad-spectrum products are used (Zehnder et al., 2007; Niggli, 2020), following an ecological systems approach to protect crops, relying more on larger biodiversity than in conventional cropping systems (Baker et al., 2020). It can be expected that the role of bioprotectants in organic farming will increase in the future if the use of copper fungicides is restricted and more emphasis will be given to the use of selective crop protection products. Main applications in this increasing market will be the control of problematic multicyclic foliar diseases unless fully resistant cultivars become available. A few potential candidates for the development of bioprotectants needed in future organic farming have been described, for example, *Lysobacter capsici* AZ778 for control of downy mildew in grapevine (Segarra et al., 2015) and *Cladosporium cladosporioides* H39 for control of apple scab (Köhl et al., 2015). Antagonistic effects of several bacteria and fungi on other downy mildews including *Phytophthora infestans* have been reported under controlled conditions but biological control of these pathogens under field conditions is still a challenge. Examples of successful biological control of diseases with particular importance for organic farming are limited. The specific biology of this group of pathogens and the resulting complex disease epidemiology with multiple cycles, rapid spread within the crop and high potential to cause yield losses in a short time period are all challenges facing the development of crop protection products, including bioprotectants.

5 Future integrated approaches

5.1 Food production within planetary boundaries

Future cropping systems should be built on closed nutrient cycles with limited use of external resources. Protection of biodiversity will be the other pillar to produce food within existing planetary boundaries (Steffen et al., 2015). Developing such new cropping systems will be a major challenge in the near future. A particular difficulty is the uncertainty of the impact of climate change on agricultural systems (Lamichhane et al., 2015). Crop protection approaches in future systems will rely on their intrinsic buffering capacity against pests and diseases. This robustness against damage by diseases will be based on functions of the plant microbiome (Berg et al., 2017; Berg et al., 2020; CAST, 2020) in combination with genetic diversification of crops and a variety of crop protection approaches, including the use of bioprotectants. With climate change, invasive pathogens may come, and the role of already indigenous pathogens may evolve. Knowledge gaps concerning the future importance of certain diseases hamper the choice of relevant targets for the new generation of bioprotectants needed for future cropping systems.

5.2 Fungicide effects on microbiomes

In the future, crop protection approaches relying on the buffering functions of resident microbiome and additional crop protection measures should not interfere with microbiome composition and function. The impact of insecticides on natural biological control has been studied extensively since the publication of *Silent Spring* by Rachel Carson in 1962. Similar information on potential fungicide effects on resident microbiomes is surprisingly scarce and scattered. The early work of Fokkema et al. (1975) demonstrated that the saprophytic microflora on cereal leaves has an important role in preventing leaf infection by *Cochliobolus sativus*. Fungicide application with non-target effects on the natural microflora interrupted the buffering capacity on the leaves, resulting in increased pathogen infection. It can be expected that such iatrogenic diseases, occurring after fungicide treatments, are more common in crops with high chemical crop protection input, but systematic research is missing.

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Seed treatments with fungicides can change the microbiome composition of the developing crop. Such non-target effects were found by Nettles et al. (2016) in multi-year field trials with maize and soybean. Fungal communities in the rhizosphere of maize and soybean were significantly affected even one month after seeding. Seed treatments also had a significant effect on endophytic fungal populations in soybean leaves.

Recent studies of the microbiome of apple bark revealed a strong effect of orchard location, tissue age and sampling time during the growing season on the general composition of bacterial and fungal microbiomes (Arrigoni et al., 2020). Fungicide applications had no global effect on microbiome composition, but the relative abundance of specific taxa significantly differed between systems with different fungicide inputs. The relative abundance of certain potential biocontrol genera, such as *Aureobasidium*, decreased in systems with low-input disease management but other potential biocontrol genera, such as *Cryptococcus*, increased. Fungicide applications have complex effects on the microbiome on wheat leaves (Knorr et al., 2019). Certain fungal groups decreased in relative abundance, whereas other groups, especially yeasts, increased significantly. Interestingly, certain fungal groups were able to multiply after fungicide treatments and filled the available space on the leaves. Gobbi et al. (2020) compared the effect of copper fungicides and a biocontrol treatment on the grapevine phyllosphere microbiome. Bacterial populations were relatively stable whereas the fungal sample showed seasonal shifts. Significant treatment effects were limited to a few fungal taxa. In a similar study, no significant effects of a treatment with penconazole (in comparison with an untreated control) were found for indigenous bacterial and fungal populations on grapevine leaves at three experimental sites in Italy (Perazzolli et al., 2014), whereas microbiome composition significantly differed between locations. Cernava et al. (2019) reported on distinct microbiome shifts by pathogen management practices for bacterial populations on tea leaves due to strong non-target effects of the treatments. At least part of the reported differences may be due to location effects, since treated and untreated leaves were sampled at distinct locations.

5.3 Interactions between bioprotectants and microbiomes

The observed changes in microbiome composition due to fungicides used for disease management may affect the resilience of cropping systems and need further attention in future research into microbiome-pesticide interactions. For the application of biological control products based on living microorganisms, similar studies are even more essential because interactions may act in two different ways. The applied bioprotectant may affect the non-target taxa of the resident microbiome, but also the resident microbiome may affect the establishment and effectiveness of the applied bioprotectant population. Studies of potential non-target effects of biocontrol agents are limited. Brimner and Boland (2003) state that released biocontrol agents have the potential to disrupt entire ecosystems because they can interfere with the native soil communities (e.g. mycorrhizal fungi) and thus may indirectly affect plant growth. Their review on investigations of interactions between mycorrhizal fungi and biocontrol isolates of *Trichoderma* spp. revealed no consistent effects of the biocontrol strains. In different studies, mycorrhizal fungi were inhibited, unaffected or stimulated in development by *Trichoderma* spp., and even antagonism of mycorrhizal fungi against *Trichoderma* spp. has been reported. Brimner and Boland (2003) also state that the host range of several hyperparasites of fungal pathogens used in biological control is not fully known and may be broader so that potentially non-target fungi may also be affected. Deising et al. (2017) expect that applied biocontrol strains may alter resident microbial consortia and may trigger the production of microbial secondary metabolites by resident microbial consortia, causing an unpredictable risk of the use of biological control. However, wherever microbial communities interact, secondary metabolites produced in situ play a role in the communication between microbial populations, including communication with newly arriving biocontrol populations. Produced locally, at low concentrations and degraded within a short time, such secondary metabolites are present in the natural environment and no additional risk following applications of biocontrol strains is expected (Koch et al., 2018; Köhl et al., 2019). Partial effects of introduced biocontrol strains on microbiome composition have been reported, but effects were short term and often negligible, such as in applications on grapevine leaves (Perazzolli et al., 2014), strawberry leaves (Sylla et al., 2013) and lettuce rhizosphere (Scherwinski et al., 2008).

Effects of the resident microbiome on microbial biocontrol agents are more obvious since the buffering capacity of microbial communities is a general phenomenon and a rich biodiversity decreases the susceptibility of ecosystems for invasion (Köhl et al., 2019; Lugtenberg, 2018; Tilman, 1999). This general ecological principle also explains the commonly observed decrease in introduced biocontrol populations (Köhl et al., 2019). The role of the resident microbiome can be demonstrated by a 'de-coupling' experiment. Disruption of the rhizosphere microbiome by the application of a broad-spectrum fungicide led to a better establishment of an introduced antagonistic *Bacillus amyloliquefaciens* isolate and resulted in stronger suppression against *Fusarium oxysporum* f. sp. *cucumerinum* in the rhizosphere soil (Qiu et al., 2014). A similar principle is applied when antagonists are introduced following soil disinfection by steaming. Increasing the resilience of the resident microbiome in future robust cropping systems may therefore affect the establishment and effectiveness of the applied bioprotectant population. For example, the antagonist *Lysobacter* *capsici* AZ78 did not establish in a vineyard with rich bacterial diversity with strong antagonistic properties (Perazzolli et al., 2014). In this study, Perazzolli et al. (2014) compared the effect of the microbiome of grapevine leaves from three different vineyards on *Plasmopora viticola* by applying leaf washings on *P. viticola*-inoculated leaf discs. The foliar microbiome from one location had a strong effect on *P. viticola* in the leaf disc assay. Application of *L. capsici* AZ78 in this vineyard did not alter the microbiome structure. However, the leaf washings from another vineyard were not effective in the leaf disc assay against the pathogen. In this vineyard, application of *L. capsici* AZ78 increased the abundance of a bacterial group (Xanthomonadaceae) that includes *L. capsici*. These findings led to the hypothesis that indigenous microbiomes with high diversity and biocontrol properties as found on the first site are more resistant to exogenous microorganisms, including the pathogen *P. viticola* and the antagonist *L. capsici*. Biocontrol effects of introduced bioprotectants therefore depend on the structure and functions of the resident microbiome. The role of the bioprotectants in this regard is changing from a general crop protection product to a product complementing resident microbiomes where needed.

5.4 Shaping microbiomes

Current microbiome research is aimed at understanding the structure and function of plant microbiomes and their role in plant health and biocontrol approaches (Berg et al., 2020). Enhancing microbial diversity was identified as a new mode of action of bioprotectants (see elsewhere in this book). Insights into the functions of the microbiome in natural biological control will allow measures to enhance the resident microbiome in order to improve its biocontrol function, similar to the support of resident natural enemies of pests, such as by adapting the architecture of the landscape or strip crops. Reports on measures implemented to shape the resident microbiome towards enhanced disease suppression are still limited. A well-studied case is the increased soil suppressiveness against take-all disease in wheat monoculture (Weller et al., 2002). Recently, rare sugars have been tested to shape the microbiome of grapevine leaves (Perazzolli et al., 2020). Tagotose (TAG) application on grapevine leaves caused significant changes in microbiome composition, leading to a relative increase in potentially beneficial indigenous microorganisms. However, since amplicon sequencing revealed information on the genus level, the beneficial functions can only be hypothesized. The microbiome composition differed between the two vineyards. The hypothesized increase in beneficial microbial groups was found in one of the two vineyards, suggesting that the effect of TAG on disease development depends on the original composition of the site-specific microbiome. The disease control effect of TAG applications under field conditions of downy mildew and, more pronounced, on powdery mildew may be a combined effect of the direct control effect via the anti-nutritional effects of this rare sugar on specific taxa, including the pathogens, and the indirect effect by shaping the microbiome towards an increased relative abundance of (hypothesized) beneficial bacterial and fungal groups. Such an engineering of phyllosphere microbiomes has potential as a new biocontrol approach.

In future cropping systems with strong emphasis on the natural buffering capacity against plant diseases of resident microbiomes in the soil and on and in plants, the role of bioprotectants will change from general crop protection to specific support of and as a complement to resident microbiomes where needed. The high specificity of the bioprotectant against certain pathogens without non-target effects on the broader microbiome will be an important requirement. The interplay of the introduced bioprotectants with the resident microbiome will occur in two ways: complementing the disease suppressiveness of the system and shaping the microbiome towards increased and stable suppressiveness.

6 Case study: the role of bioprotectants in different apple scab control approaches

6.1 Apple scab epidemiology and control

Apple scab caused by *Venturia inaequalis* is the most prevalent apple disease worldwide. The pathogen affects leaves and fruits leading to losses in fruit yield and quality (MacHardy et al., 2001). The multicyclic epidemic starts in spring with the release of ascospores from overwintering apple leaves on the orchard floor. This primary inoculum is present in the orchard during just a few weeks in spring and infects young, highly susceptible developing leaves and young fruits. In a second phase of the epidemic, *V. inaequalis* produces conidia on scabbed leaf tissue during the remaining growing season, which can infect leaves and fruits in multiple infection-sporulation cycles. Young leaves formed during summer are a driving force of the summer epidemic since they are highly susceptible.

Current scab management relies on multiple applications of fungicides, often guided by sophisticated DSS, combining forecasting risks of infection periods, susceptibility of apple tissues and fungicide coverage from earlier applications. Multiple applications of copper-based fungicides or other certified crop protection products are common in organic apple production.

Two strategies for biological control of apple scab have been explored. Antagonists have been selected to interfere with the surviving mycelium and production of fruiting bodies in fallen leaves during the winter season on the orchard floor. The objective of this biocontrol strategy is to reduce the number of ascospores released from pseudothecia in spring so that the primary infections of developing leaves and fruits by ascospores are reduced. The antagonistic fungi *Athelia bombacina* (Heye and Andrews, 1983) and *Microsphaeropsis* sp. (Carisse et al., 2000) have been selected for this purpose. Carisse et al. (2000) showed that autumn applications of *Microsphaeropsis* sp. on the orchard floor reduced the number of ascospores produced by *V. inaequalis* by 70–80% so that the number of fungicide sprays needed for scab control during the growing season could be reduced. In the second biocontrol strategy, antagonists are applied during the growing season to the canopy to prevent initial infections by ascospores in spring or further spread of scab by conidia during the summer epidemic. Several screening programmes have been reported and resulted in a few candidates for biocontrol products, for example, *Chaetomium globosum* (Boudreau and Andrews, 1987), *Pseudomonas syringae* (Burr et al., 1996), epiphytic yeasts (Fiss et al., 2000) and *Cladosporium cladosporioides* (Köhl et al., 2009, 2015).

Apple fruits are produced in cropping systems with different integrated crop protection approaches (Caffi et al., 2017; Holb et al., 2017). Growers' choices depend on their economic and environmental concerns, their risk strategies concerning yield and quality losses and market prices for fruits produced under different systems (Pissonnier et al., 2016). Conventional systems mainly rely on regular applications of synthetic fungicides, whilst IPM systems use DSS before fungicides are applied and often integrate further measures to reduce apple scab risks, such as sanitation and resistant varieties – if marketing of such varieties is feasible. A limited number of fungicide applications is advised in orchards with resistant varieties to prevent the development of *V. inaequalis* populations from breaking this resistance against the pathogen. Organic cropping systems rely on applications of fungicides certified for use in organic farming, such as copper compounds and sulphur, often in combination with resistant varieties (Speiser et al., 2014). Future resilient cropping systems may be developed that fully exploit the benefits of resident microbiomes in scab-resistant varieties. Options for careful microbiome modulation may also become available to protect the crop from damage by the pathogen (Perazzolli et al., 2020). In such future apple cropping systems, interventions with crop protection products will be limited to exceptional periods of predicted high and unacceptable risks for yield and quality losses.

6.2 Bioprotectants in conventional systems

Bioprotectants with the potential to reduce ascospore production before the growing season and to control the progress of scab epidemics during the growing season could have different positioning in spray schedules in cropping systems with different crop protection approaches. In conventional approaches, regular fungicide applications are common, and often applied as calendar sprays, especially if applied by agricultural contractors (Fig. 2a).

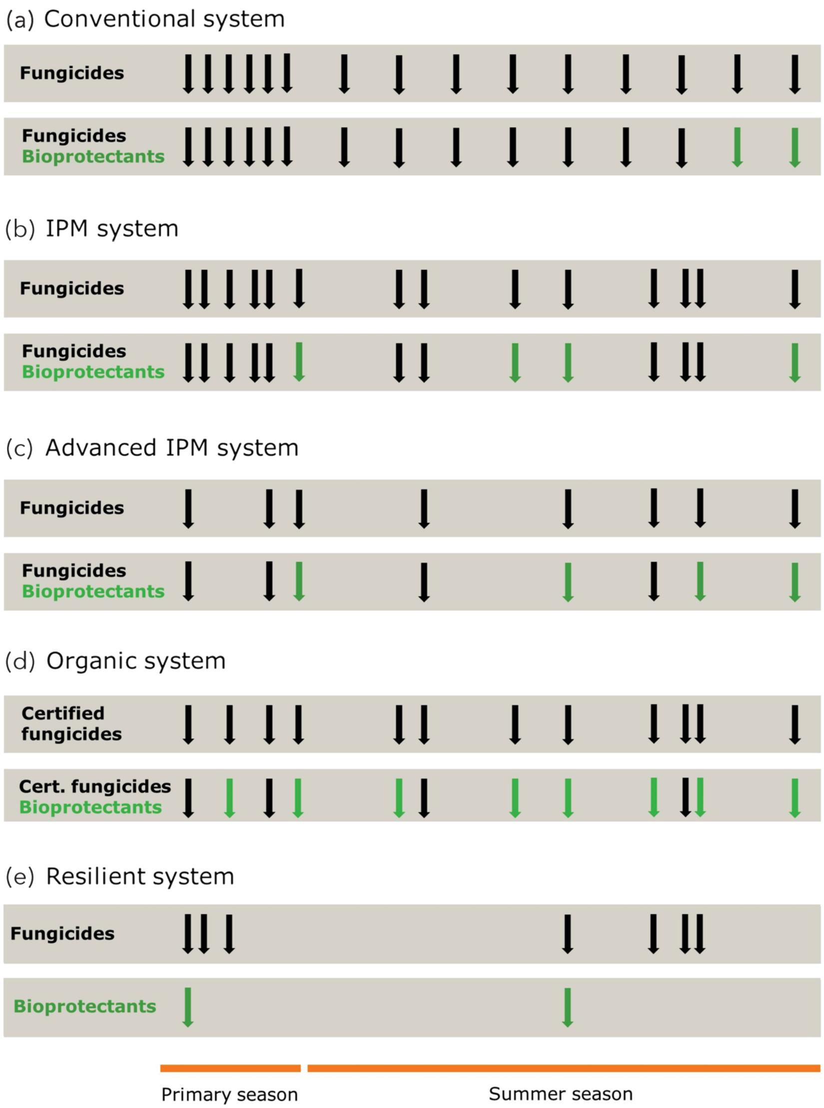

Figure 2 Integration of bioprotectants for apple scab control in different cropping systems. Application of chemical fungicides indicated by black arrows and bioprotectants by green arrows. Preventative measures and bioprotectants targeting leaf litter during the winter season in advanced IPM systems and organic systems not shown. (a) conventional cropping system; (b) IPM system; (c) advanced IPM system; (d) organic cropping system; (e) resilient cropping system.

Options for integration of biocontrol products into such crop protection approaches may be limited. Risks of selection of resistance against the key systemic fungicides within the pathogen populations may be counteracted by using different synthetic fungicides in alternation. The main reason to apply a biocontrol product is to limit the residue level on the marketed fruits below that accepted by distributors and retailers. In this situation, the biocontrol product will replace one or a few late season applications of fungicides against scab, if the biocontrol product can be integrated into spray schedules with applications of fungicides against various apple fruit rots usually applied late in the season.

6.3 Bioprotectants in integrated pest management systems

In IPM systems, fungicide applications for scab control are guided by DSS considering forecasted risks of potential infection periods and expected leaf coverage with fungicides applied during earlier treatments (Fig. 2b). Calendar applications of fungicides are avoided. The choice of a specific fungicide depends on the infection risk level and the number of applications of certain fungicides if their application frequency is limited to prevent build-up of fungicide resistance in the pathogen population. In such a management strategy, a biocontrol product – with possibly lower or more variable efficacy compared to the most effective fungicides – can be integrated during the entire growing season. The biocontrol product can be applied before forecasted moderate or low infection risk periods instead of fungicides to reduce unwanted environmental side effects of the applied spray schedule and to avoid multiple applications of fungicides at risk of resistance development. Depending on the development of the scab epidemic and the weather conditions during the season, several fungicide applications can be replaced by the biocontrol product during the primary season and the summer epidemic. Since developing young leaves are the driving force of the summer epidemic, fungicides present on older leaves from earlier applications may not interfere with the efficacy of the applied antagonist on the young leaves, allowing a flexible integration into spray schedules with alternating chemical and biological control applications. At the end of the season, applications of the biocontrol product will be preferred to achieve low residue levels on the harvested fruits.

In more advanced IPM systems, the use of DSS is complemented by various preventative measures. To reduce the risk of primary infections in the following spring, sanitation measures such as the physical removal of fallen leaves on the orchard floor or the enhancement of their decomposition by shredding or urea application (Gomez et al., 2007; Sutton et al., 2000) can be complemented or replaced by treatments with antagonists such as *Microsphaeropsis* sp. selected for their competitive ability in necrotic leaf tissues (Carisse et al., 2000). Another option is the use of scab-resistant varieties. In orchards planted with common resistant varieties, fungicide treatments applied several times during the growing season are recommended to prevent breaking of scab-resistance by local *V. inaequalis* populations (Jamar and Lateur, 2007). Such fungicide treatments can potentially be replaced by applications of bioprotectants. If scab epidemics develop in such IPM systems, their management by fungicide treatment is guided by DSS. Since the disease pressure will generally be lower, more fungicide treatments can be replaced by biocontrol products compared to less advanced IPM systems or in conventional systems (Fig. 2c).

6.4 Bioprotectants in organic systems

In organic cropping systems, the decomposition of fallen leaves is favoured by the rich biodiversity in organically managed soils. The interplay of mesofauna and microbiome reduces in this way the overwintering potential of *V. inaequalis* in leaf litter. Physical sanitation measures that enhance leaf decomposition (Gomez et al., 2007; Sutton et al., 2000) or removal of fallen leaves by specially designed leaf vacuum machinery (Benduhn et al., 2014) further lower the ascospore load at the beginning of the growing season. Examples of future biological control options in leaf litter include yeast extracts of *Saccharomyces cerivisiae* (Porsche et al., 2017) or antagonists such as *Microsphaeropsis* sp. (Carisse et al., 2000). This combination of enhanced leaf decomposition with a rich biodiversity and additional measures generally results in lower scab pressure at the beginning of the growing season compared to conventional or IPM cropping systems. During the growing season, mainly copper fungicides are applied, guided by DSS (Fig. 2d). Copper spray schedules are complemented by applications of other fungicides accepted in organic farming such as wettable sulphur, lime sulphur and potassium bicarbonates (Jamar and Lateur, 2007). Use of copper fungicides is limited due to environmental considerations, increasingly restricting the amounts applied per hectare and season due to governmental regulations, phytotoxicity and russeting caused in certain developmental stages of apple fruits. Biocontrol products as alternatives can be positioned in the primary season to complement and increasingly replace copper fungicides. Furthermore, pathogen-specific biological control products can replace a substantial number of other organic fungicides, often with broad-spectrum activities, scheduled in the summer season. In this way, the buffering capacity of an undisturbed microbiome on leaves and fruits may reduce scab severities and support the effects of specific biocontrol products.

6.5 Bioprotectants in resilient cropping systems

Future – still partly hypothetical – highly resilient cropping systems combining resistant cultivars with the full employment of microbiota in soil and in and on plants will be less susceptible to apple scab. Interference with crop protection measures will only be needed during forecasted periods of high infection risks, combining favourable weather conditions with high inoculum pressure in the orchard (Fig. 2e). In this situation, applications of broad-spectrum fungicides, as currently used in conventional and organic apple cropping systems, may have unwanted side effects on key species of the resident microbiota and may be detrimental because they may disturb the resilience of the system. If such disturbed systems do not recover before new infection periods occur, subsequent fungicide applications are needed even during periods of lower infection risks. Disturbance may continue and even progress during a longer period – sometimes even the entire growing season – due to an iatrogenic mechanism. Selective biological control products with no or limited effects on resident microbiota will have a clear advantage. Since the resilience of the systems will not be affected by the product, single sprays during periods with high infection risks will be sufficient to support the resident microbiota. The remaining resilience of the system will sufficiently suppress further scab development during low and moderate risk periods, whereas additional subsequent treatments with the biological control product are only needed again during further high-risk periods. In this way, just a few crop protection measures will be needed during a season, and scab management will mainly rely on the functions of undisturbed resident microbiota.

7 Conclusions and future trends in research

Bioprotectants have the potential to replace chemical fungicides in all agricultural cropping systems and crop protection approaches. The development of new bioprotectants in combination with more restricted use of chemical crop protection (due to environmental considerations and a lack of available new lead products) will result in bioprotectants having a stronger market position in the future.

Bioprotectants fulfil particular roles in current and future crop protection approaches, primarily reducing pesticide residues in harvested products in conventional systems, being the first and preferred control option in IPM systems and organic farming, and complementing resident microbiomes in future resilient cropping systems.

Various barriers to adoption have been identified that will slow down the broad exploitation of bioprotectants, such as a lack of biocontrol solutions for multiple diseases in crops, high registration costs, exclusion of external costs of crop protection products, a highly competitive marketplace, risk-averse customers, complex selling channels, insufficient information and training for farmers and insufficient consideration of socioeconomic factors (Marrone, 2009; Barzman et al., 2015; Lamichhane et al., 2017; Baker et al., 2020; Zaki et al., 2020). The importance of such barriers obviously also differs for the different crop protection approaches and the related roles of bioprotectants in such approaches. The main drivers encouraging the use of bioprotectants at present are the economic advantages of the individual biocontrol product over conventional products. For envisaged future crop protection approaches, relying heavily on the resilience of the cropping system against plant diseases, new drivers for using bioprotectants will evolve. A main driver will be the selectivity of bioprotectants for use against specific problematic pathogens without non-target effects and their potential to shape resident microbiomes in their functions. There will be substantial need for such bioprotectants to safeguard the transition from current cropping systems towards resilient cropping systems without unwanted interference within the core microbiome. In this situation, incentives for development and use of bioprotectants need to change from market-driven economic incentives to a more holistic view of the true costs and benefits, including currently externalized costs for the use of different external inputs in agriculture.

8 Where to look for further information

Three international journals specifically focusing on biological control (*BioControl, Biocontrol Science and Technology, Biological Control*) publish results of scientific research on biological control of pest and plant pathogens with an increasing portion of articles on plant pathogens. However, a significant number of scientific papers on biological control of plant pathogens is published in a broad range of scientific journals on plant pathology, microbial ecology and soil microbiology, and in crop-specific journals and journals on post-harvest technologies.

The International Organisation for Biological and Integrated Control (IOBC) (www.iobc-global.org) plays an important role in the communication of scientific results on biological control and their integrated use in cropping systems. The IOBC is organized globally with different regional sections. Within the West Palaearctic Regional Section of IOBC (IOBC-WPRS) (www.iobc-wprs.org) several working groups deal with the biological control of plant pathogens, such as WG 'Biological and integrated control of plant pathogens', WG 'Induced resistance in plants against insects and diseases', WG 'Integrated protection of fruit crops' with subgroups on 'Pome fruit diseases', 'Stone fruits' and 'Soft fruits', and WG 'Integrated protection in viticulture' with the subgroup 'Fungal, bacterial and physiological diseases'.

The working groups meet on a regular basis, usually bi-yearly, with international participation of non-members as well. Contributions to the workshops are published in the *IOBC-WPRS Bulletin*. These bulletins publish scientific reports on ongoing research and technical papers related to the practical use of biological control in cropping systems. IOBC-WPRS also publishes on the frameworks for integrated production and general technical guidelines and crop specific guidelines for the implementation of integrated production and IPM.

The website of the International Biocontrol Manufacturers Association (IBMA; www.ibma-global.org) informs about commercial development, registration and marketing of biocontrol products. The IBMA organizes annually a global biocontrol industry meeting to network, discover and unveil new products, market opportunities and research areas and inform policy makers and regulators of the specific needs of the biocontrol industry. The website (www.abim.ch) includes an informative archive of presentations held during the meetings since 2006.

9 References

Arrigoni, E., Albanese, D., Longa, C. M. O., Angeli, D., Donati, C., Ioriatti, C., Pertot, I. and Perazzolli, M. (2020). Tissue age, orchard location and disease management influence the composition of fungal and bacterial communities present on the bark of apple trees, *Environ. Microbiol.* 22(6), 2080–2093.

Baker, B. P., Green, T. A. and Loker, A. J. (2020). Biological control and integrated pest management in organic and conventional systems, *Biol. Control* 140, 104095.

Bakker, P. A. H. M., Berendsen, R. L., Van Pelt, J. A., Vismans, G., Yu, K., Li, E., Van Bentum, S., Poppeliers, S. W. M., Sanchez Gil, J. J., Zhang, H., Goossens, P., Stringlis, I. A., Song, Y., de Jonge, R. and Pieterse, C. M. J. (2020). The soil-borne identity and microbiome-assisted agriculture: looking back to the future, *Mol. Plant* 13(10), 1394–1401.

Barzman, M., Bàrberi, P., Birch, A. N. E., Boonekamp, P., Dachbrodt-Saaydeh, S., Graf, B., Hommel, B., Jensen, J. E., Kiss, J., Kudsk, P., Lamichhane, J. R., Messéan, A., Moonen, A.-C., Ratnadass, A., Ricci, P., Sarah, J.-L. and Sattin, M. (2015). Eight principles of integrated pest management, *Agron. Sustain. Dev.* 35(4), 1199–1215. DOI: 10.1007/s13593-015-0327-9.

Beillouin, D., Ben-Ari, T. and Makowski, D. (2019). Evidence map of crop diversification strategies at the global scale, *Environ. Res. Lett.* 14(12), 123001.

Benduhn, B., Zimmer, J. and Buchleither, S. (2014). Effect of mechanically removing of leaf litter on apple scab (Venturia inaequalis) infestation in organic apple production. In: Foerdergemeinschaft Oekologischer Obstbau e.V. (Ed), Eco-Fruit: Proc. 17th Int. Conf. Organic Fruit Growing, Hohenheim, Germany, pp. 40–44.

Berg, G., Köberl, M., Rybakova, D., Müller, H., Grosch, R. and Smalla, K. (2017). Plant microbial diversity is suggested as the key to future biocontrol and health trends, *FEMS Microbiol. Ecol.* 93(5), fix050.

Berg, G., Rybakova, D., Fischer, D., Cernava, T., Vergès, M.-C. C., Charles, T., Chen, X., Cocolin, L., Eversole, K., Corral, G. H., Kazou, M., Kinkel, L., Lange, L., Lima, N., Loy, A., Macklin, J. A., Maguin, E., Mauchline, T., McClure, R., Mitter, B., Ryan, M., Sarand, I., Smidt, H., Schelkle, B., Roume, H., Kiran, G. S., Selvin, J., Souza, R. S. C. D., Van Overbeek, L., Singh, B. K., Wagner, M., Walsh, A., Sessitsch, A. and Schloter, M. (2020). Microbiome definition re-visited: old concepts and new challenges, *Microbiome* 8(1), 103.

Boudreau, M. A. and Andrews, J. H. (1987). Factors influencing antagonism of *Chaetomium globosum* to *Venturia inaequalis*: a case study in failed biocontrol, *Phytopathology* 77(10), 1470–1475.

Bourguet, D. and Guillemaud, T. (2016). The hidden and external costs of pesticide use. In: Lichtfouse, E. (Ed), *Sustainable Agriculture Reviews* (vol. 19), Springer, pp. 35–120.

Brimner, T. A. and Boland, G. J. (2003). A review of the non-target effects of fungi used to biologically control plant diseases, *Agric. Ecosyst. Environ.* 100(1), 3–16.

Burr, T. J., Matteson, M. C., Smith, C. A., Corral-Garcia, M. R. and Huang, T.-C. (1996). Effectiveness of bacteria and yeasts from apple orchards as biological control agents of apple scab, *Biol. Control* 6(2), 151–157.

Buurma, J. S., Lamine, C. and Haynes, I. (2012). Transition to consumer driven value chains in the Netherlands, *Acta Hortic.* (930), 69–75.

Caffi, T., Helsen, H. H. M., Rossi, V., Holb, I. J., Strassemeyer, J., Buurma, J. S., Capowiez, Y., Simon, S. and Alaphilippe, A. (2017). Multicriteria evaluation of innovative IPM systems in pome fruit in Europe, *Crop Prot.* 97, 101–108.

Carisse, O., Philion, V., Rolland, D. and Bernier, J. (2000). Effect of fall application of fungal antagonist on spring ascospore production of the apple scab pathogen, *Venturia inaequalis*, *Phytopathology* 90(1), 31–37.

CAST (Council for Agricultural Science and Technology). (2020). Agriculture and the Microbiome. Issue Paper 68, CAST: Ames, IA.

Cernava, T., Chen, X., Krug, L., Li, H., Yang, M. and Berg, G. (2019). The tea leaf microbiome shows specific responses to chemical pesticides and biocontrol applications, *Sci. Total Environ.* 667, 33–40.

Dainese, M., Martin, E. A., Aizen, M. A., Albrecht, M., Bartomeus, I., Bommarco, R., Carvalheiro, L. G., Chaplin-Kramer, R., Gagic, V., Garibaldi, L. A., Ghazoul, J., Grab, H., Jonsson, M., Karp, D. S., Kennedy, C. M., Kleijn, D., Kremen, C., Landis, D. A., Letourneau, D. K., Marini, L., Poveda, K., Rader, R., Smith, H. G., Tscharntke, T., Andersson, G. K. S., Badenhausser, I., Baensch, S., Bezerra, A. D. M., Bianchi, F. J. J. A., Boreux, V., Bretagnolle, V., Caballero-Lopez, B., Cavigliasso, P., Ćetković, A., Chacoff, N. P., Classen, A., Cusser, S., da Silva E Silva, F. D., de Groot, G. A., Dudenhöffer, J. H., Ekroos, J., Fijen, T., Franck, P., Freitas, B. M., Garratt, M. P. D., Gratton, C., Hipólito, J., Holzschuh, A., Hunt, L., Iverson, A. L., Jha, S., Keasar, T., Kim, T. N., Kishinevsky, M., Klatt, B. K., Klein, A. M., Krewenka, K. M., Krishnan, S., Larsen, A. E., Lavigne, C., Liere, H., Maas, B., Mallinger, R. E., Martinez Pachon, E., Martínez-Salinas, A., Meehan, T. D., Mitchell, M. G. E., Molina, G. A. R., Nesper, M., Nilsson, L., O'Rourke, M. E., Peters, M. K., Plećaš, M., Potts, S. G., Ramos, D. L., Rosenheim, J. A., Rundlöf, M., Rusch, A., Sáez, A., Scheper, J., Schleuning, M., Schmack, J. M., Sciligo, A. R., Seymour, C., Stanley, D. A., Stewart, R., Stout, J. C., Sutter, L., Takada, M. B., Taki, H., Tamburini, G., Tschumi, M., Viana, B. F., Westphal, C., Willcox, B. K., Wratten, S. D., Yoshioka, A., Zaragoza-Trello, C., Zhang, W., Zou, Y. and Steffan-Dewenter, I. (2019). A global synthesis reveals biodiversity-mediated benefits for crop production, *Sci. Adv.* 5(10), art. no. eaax0121.

Deising, H. B., Gase, I. and Kubo, Y. (2017). The unpredictable risk imposed by microbial secondary metabolites: how safe is biological control of plant diseases?, *J. Plant Dis. Prot.* 124(5), 413–419.

Ditzler, L., van Apeldoorn, D. Fv, Schulte, R. P. O., Tittonell, P. and Rossing, W. A. H. (2021). Redefining the field to mobilize three-dimensional diversity and ecosystem services on the arable farm, *Eur. J. Agron.* 122, 126197.

Eilenberg, J., Hajek, A. and Lomer, C. (2001). Suggestions for unifying the terminology in biological control, *BioControl* 46(4), 387–400.

European Commission. (2007). Council Regulation (EC) No 834/2007 of 28 June 2007 on organic production and labelling of organic products and repealing Regulation (EEC) No 2092/91. Off. J. Eur. Union L189, 1–23.

European Commission. (2008). Commission regulation (EC) No 889/2008 of 5 September 2008, laying down detailed rules for the implementation of Council Regulation (EC) No 834/2007 on organic production and labelling of organic products with regard to organic production, labelling and control. Off. J. Eur. Commun. L 250/1, 1–84.

European Parliament. (2009). Directive 2009/128/EC of the European Parliament and of the council of 21 October 2009 establishing a framework for community action to achieve the sustainable use of pesticides, *Off. J. Eur. Union* 309, 71–86.

Fiss, M., Kucheryava, N., Schönherr, J., Kollar, A., Arnold, G. and Auling, G. (2000). Isolation and characterization of epiphytic fungi from the phyllosphere of apple as potential biocontrol agents against apple scab (*Venturia inaequalis*), *Z. Pflanzenkr. Pflanzenschutz J. Plant Dis. Prot.* 107(1), 1–11.

Fokkema, N. J., van de Laar, J. A. J., Nelis-Blomberg, A. L. and Schippers, B. (1975). The buffering capacity of the natural mycoflora of rye leaves to infection by *Cochliobolus sativus*, and its susceptibility to benomyl, *Nether. J. Plant Pathol.* 81(5), 176–186.

Gerlagh, M., Goossen-Van De Geijn, H. M., Fokkema, N. J. and Vereijken, P. F. G. (1999). Long-term biosanitation by application of *Coniothyrium minitans* on *Sclerotinia sclerotiorum*-infected crops, *Phytopathology* 89(2), 141–147.

Gobbi, A., Kyrkou, I., Filippi, E., Ellegaard-Jensen, L. and Hansen, L. H. (2020). Seasonal epiphytic microbial dynamics on grapevine leaves under biocontrol and copper fungicide treatments, *Sci. Rep.* 10(1), art. no. 681.

Gomez, C., Brun, L., Chauffour, D. and de Le Vallee, D. D. L. (2007). Effect of leaf litter management on scab development in an organic apple orchard, *Agri. Ecosyst. Environ.* 118(1–4), 249–255.

Heimpel, G. E. and Mills, N. (2017). *Biological Control—Ecology and Applications*, Cambridge University Press: Cambridge.

Heye, C. C. and Andrews, J. H. (1983). Antagonism of *Athelia bombacina* and *Chaetomium globosum* to the apple scab pathogen, *Venturia inaequalis*, *Phytopathology* 73(5), 650–654.

Holb, I. J., Abonyi, F., Buurma, J. and Heijne, B. (2017). On-farm and on-station evaluations of three orchard management approaches against apple scab and apple powdery mildew, *Crop Prot.* 97, 109–118.

Jamar, L. and Lateur, M. (2007). Strategies to reduce copper use in organic apple production, *Acta Hortic.* 737(737), 113–120.

Kerdraon, L., Laval, V. and Suffert, F. (2019). Microbiomes and pathogen survival in crop residues, an ecotone between plant and soil, *Phytobiomes J.* 3(4), 246–255.

Knorr, K., Jørgensen, L. N. and Nicolaisen, M. (2019). Fungicides have complex effects on the wheat phyllosphere mycobiome, *PLoS ONE* 14(3), art. no. e0213176.

Koch, E., Becker, J. O., Berg, G., Hauschild, R., Jehle, J., Köhl, J. and Smalla, K. (2018). Biocontrol of plant diseases is not an unsafe technology!, *J. Plant Dis. Prot.* 125(2), 121–125.

Köhl, J., Haas, B. H., Kastelein, P., Burgers, S. L. G. E. and Waalwijk, C. (2007). Population dynamics of *Fusarium* spp. and *Microdochium nivale* in crops and crop residues of winter wheat, *Phytopathology* 97(8), 971–978.

Köhl, J., Kolnaar, R. and Ravensberg, W. J. (2019). Mode of action of microbial biological control agents against plant diseases: relevance beyond efficacy, *Front. Plant Sci.* 10, 845.

Köhl, J. J., Molhoek, W. W. M. L., Groenenboom-de Haas, B. B. H. and Goossen-van de Geijn, H. H. M. (2009). Selection and orchard testing of antagonists suppressing conidia production of the apple scab pathogen *Venturia inaequalis*, *Eur. J. Plant Pathol.* 123(4), 401–414.

Köhl, J., Scheer, C., Holb, I. J., Masny, S. and Molhoek, W. M. L. (2015). Towards an integrated use of biological control by *Cladosporium cladosporioides* H39 in apple scab (*Venturia inaequalis*) management, *Plant Dis.* 99(4), 535–543.

Lamichhane, J. R., Barzman, M., Booij, K., Boonekamp, P., Desneux, N., Huber, L., Kudsk, P., Langrell, S. R. H., Ratnadass, A., Ricci, P., Sarah, J. L. and Messéan, A. (2015). Robust cropping systems to tackle pests under climate change: a review, *Agron. Sustain. Dev.* 35(2), 443–459.

Lamichhane, J. R., Bischoff-Schaefer, M., Bluemel, S., Dachbrodt-Saaydeh, S., Dreux, L., Jansen, J. P., Kiss, J., Köhl, J., Kudsk, P., Malausa, T., Messéan, A., Nicot, P. C., Ricci, P., Thibierge, J. and Villeneuve, F. (2017). Identifying obstacles and ranking common biological control research priorities for Europe to manage most economically important pests in arable, vegetable and perennial crops, *Pest Manag. Sci.* 73(1), 14–21.

Lamichhane, J. R., Osdaghi, E., Behlau, F., Köhl, J., Jeffrey, B., Jones, J. B. and Aubertot, J.-N. (2018). Thirteen decades of anti-microbial copper compounds applied in agriculture: a review, *Agron. Sustain. Dev.* 38(3), 38–28.

Lugtenberg, B. (2018). Putting concerns for caution into perspective: microbial plant protection products are safe to use in agriculture, *J. Plant Dis. Prot.* 125(2), 127–129.

MacHardy, W. E., Gadoury, D. M. and Gessler, C. (2001). Parasitic and biological fitness of *Venturia inaequalis*: relationship to disease management strategies, *Plant Dis.* 85(10), 1036–1051.

Marrone, P. G. (2009). Barriers to adoption of biological control agents and biological pesticides. In: Radcliffe, E. B., Hutchison, W. D. and Cancelado, R. E. (Eds), *Integrated Pest Management*, Cambridge University Press, pp 163–178.

Meissle, M., Romeis, J. and Bigler, F. (2011). Bt maize and integrated pest management – a European perspective, *Pest Manag. Sci.* 67(9), 1049–1058.

Muller, A., Schader, C., El-Hage Scialabba, N., Brüggemann, J., Isensee, A., Erb, K. H., Smith, P., Klocke, P., Leiber, F., Stolze, M. and Niggli, U. (2017). Strategies for feeding the world more sustainably with organic agriculture, *Nat. Commun.* 8(1), 1290. DOI: 10.1038/s41467-017-01410-w.

Nettles, R., Watkins, J., Ricks, K., Boyer, M., Licht, M., Atwood, L. W., Peoples, M., Smith, R. G., Mortensen, D. A. and Koide, R. T. (2016). Influence of pesticide seed treatments on rhizosphere fungal and bacterial communities and leaf fungal endophyte communities in maize and soybean, *Appl. Soil Ecol.* 102, 61–69.

Niggli, U. (2020). Plant protection in agroecological farming systems, *Agroscope Nachhaltigkeitstagung*, 23 January 2020. Available at: https://www.agroscope.admin.ch/agroscope/de/home/aktuell/veranstaltungen/nachhaltigkeitstagung/fruehere-praesentationen.html#-862383929 Visited 23-03-2021.

Niu, B., Wang, W., Yuan, Z., Sederoff, R. R., Sederoff, H., Chiang, V. L. and Borriss, R. (2020). Microbial interactions within multiple-strain biological control agents impact soil-borne plant disease, *Front. Microbiol.* 11, 585404.

Oerke, E.-C., Dehne, H.-W., Schönbeck, F. and Weber, A. (1994). *Crop Production and Crop Protection - Estimated Losses in Major Food and Cash Crops*, Elsevier Science: Amsterdam.

Perazzolli, M., Antonielli, L., Storari, M., Puopolo, G., Pancher, M., Giovannini, O., Pindo, M. and Pertot, I. (2014). Resilience of the natural phyllosphere microbiota of the grapevine to chemical and biological pesticides, *Appl. Environ. Microbiol.* 80(12), 3585–3596.

Perazzolli, M., Nesler, A., Giovannini, O., Antonielli, L., Puopolo, G. and Pertot, I. (2020). Ecological impact of a rare sugar on grapevine phyllosphere microbial communities, *Microbiol. Res.* 232, 126387.

Pimentel, D. and Burgess, M. (2014a). Environmental and economic costs of the application of pesticides primarily in the United States. In: Pimentel, D., and Peshin, R. (Eds), *Integrated Pest Management*, Springer Science+Business Media: Dordrecht, pp 48–71.

Pimentel, D. and Burgess, M. (2014b). Environmental and economic benefits of reducing pesticide use. In: Pimentel, D., and Peshin, R. (Eds), *Integrated Pest Management*, Springer Science+Business Media: Dordrecht, pp 128–139.

Pissonnier, S., Lavigne, C., Toubon, J.-F. and Le Gal, P.-Y. (2016). Factors driving growers' selection and implementation of an apple crop protection strategy at the farm level, *Crop Prot.* 88, 109–117.

Porsche, F. M., Pfeiffer, B. and Kollar, A. (2017). A new phytosanitary method to reduce the ascospore potential of *Venturia inaequalis*, *Plant Dis.* 101(3), 414–420.

Qiu, M., Li, S., Zhou, X., Cui, X., Vivanco, J. M., Zhang, N., Shen, Q. and Zhang, R. (2014). De-coupling of root–microbiome associations followed by antagonist inoculation improves rhizosphere soil suppressiveness, *Biol. Fertil. Soils* 50(2), 217–224.

Scherwinski, K., Grosch, R. and Berg, G. (2008). Effect of bacterial antagonists on lettuce: active biocontrol of Rhizoctonia solani and negligible, short-term effects on nontarget microorganisms, *FEMS Microbiol. Ecol.* 64(1), 106–116.

Segarra, G., Puopolo, G., Giovannini, O. and Pertot, I. (2015). Stepwise flow diagram for the development of formulations of non spore-forming bacteria against foliar pathogens: the case of Lysobacter capsici AZ78, *J. Biotechnol.* 216, 56–64.

Speiser, B. and Tamm, L. (2011). Regulation of plant protection in organic farming. In: Ehlers, R.-U. (Ed), *Regulation of Biological Control Agents*, Springer: Dordrecht Heidelberg London New York, pp 113–125.

Speiser, B., Tamm, L. and Weibel, F. P. (2014). Regulatory framework for plant protection in organic farming. In: Bellon, S. and Penvern, S. (Eds), *Organic Farming, Prototype for Sustainable Agricultures*, Springer Science+Business Media: Dordrecht, pp 65–82.

Steffen, W., Richardson, K., Rockström, J., Cornell, S. E., Fetzer, I., Bennett, E. M., Biggs, R., Carpenter, S. R., De Vries, W., De Wit, C. A., Folke, C., Gerten, D., Heinke, J., Mace, G. M., Persson, L. M., Ramanathan, V., Reyers, B. and Sörlin, S. (2015). Sustainability. Planetary boundaries: guiding human development on a changing planet, *Science* 347(6223), art. no. 1259855.

Stenberg, J. A., Sundh, I., Becher, P. G., Björkman, C., Dubey, M., Egan, P. A., Friberg, H., Gil, J. F., Jensen, D. F., Jonsson, M., Karlsson, M., Khalil, S., Ninkovic, V., Rehermann, G., Vetukuri, R. R. and Viketoft, M. (2021). When is it biological control? A framework of definitions, mechanisms, and classifications, *J. Pest Sci.* 94(3), 665–676, DOI: 10.1007/s10340-021-01354-7.

Sutton, D. K., MacHardy, W. E. and Lord, W. G. (2000). Effects of shredding or treating apple leaf litter with urea on ascospore dose of *Venturia inaequalis* and disease buildup, *Plant Dis.* 84(12), 1319–1326.

Syed Ab Rahman, S. F., Singh, E., Pieterse, C. M. J. and Schenk, P. M. (2018). Emerging microbial biocontrol strategies for plant pathogens, *Plant Sci.* 267, 102–111. DOI: 10.1016/j.plantsci.2017.11.012.

Sylla, J., Alsanius, B. W., Kruger, E., Reineke, A., Strohmeier, S. and Wohanka, W. (2013). Leaf microbiota of strawberries as affected by biological control agents, *Phytopathology* 103(10), 1001–1011.

Tilman, D. (1999). The ecological consequences of changes in biodiversity: a search for general principles, *Ecology* 80, 1455–1474.

United States Dept. Agric. (USDA). (2011). National organic program handbook, United States Department of Agriculture Agric. Mark. Serv: Washington, DC.

Van Bruggen, A. H. C. and Finckh, M. R. (2016). Plant diseases and management approaches in organic farming systems, *Annu. Rev. Phytopathol.* 54, 25–54.

Van Bruggen, A. H. C., Gamliel, A. and Finckh, M. R. (2016). Plant disease management in organic farming systems, *Pest Manag. Sci.* 72(1), 30–44.

Van Selm, B., de Boer, I. J. M., van Ittersum, M. K., Hijbeek, R. and van Zanten, H. H. E. (2020). Alternative futures of circular food systems: the environmental consequences of adopting circularity at different spatial scales. In: WIAS Annual Conference 2020: Frontiers in Animal Sciences, WIAS, pp. 57–57.

Van Zanten, H. H. E., Van Ittersum, M. K. and De Boer, I. J. M. (2019). The role of farm animals in a circular food system, *Glob. Food Sec.* 21, 18–22.

Weller, D. M., Raaijmakers, J. M., Gardener, B. B. and Thomashow, L. S. (2002). Microbial populations responsible for specific soil suppressiveness to plant pathogens, *Annu. Rev. Phytopathol.* 40, 309–348.

Willett, W., Rockström, J., Loken, B., Springmann, M., Lang, T., Vermeulen, S., Garnett, T., Tilman, D., DeClerck, F., Wood, A., Jonell, M., Clark, M., Gordon, L. J., Fanzo, J., Hawkes, C., Zurayk, R., Rivera, J. A., De Vries, W., Majele Sibanda, L., Afshin, A., Chaudhary, A., Herrero, M., Agustina, R., Branca, F., Lartey, A., Fan, S., Crona, B., Fox, E., Bignet, V., Troell, M., Lindahl, T., Singh, S., Cornell, S. E., Srinath Reddy, K., Narain, S., Nishtar, S. and Murray, C. J. L. (2019). Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems, *Lancet* 393(10170), 447–492.

Zaki, O., Weekers, F., Thonart, P., Tesch, E., Kuenemann, P. and Jacques, P. (2020). Limiting factors of mycopesticide development, *Biol. Control* 144, art. no. 104220.

Zehnder, G., Gurr, G. M., Kühne, S., Wade, M. R., Wratten, S. D. and Wyss, E. (2007). Arthropod pest management in organic crops, *Annu. Rev. Entomol.* 52(1), 57–80.

Zeng, W., Kirk, W. and Hao, J. (2012). Field management of Sclerotinia stem rot of soybean using biological control agents, *Biol. Control* 60(2), 141–147.