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Streptomyces competition and co-evolution in relation to plant disease suppression

Linda L. Kinkel [a,*], Daniel C. Schlatter [a], Matthew G. Bakker [b], Brett E. Arenz [a]

[a] Department of Plant Pathology, University of Minnesota, 495 Borlaug Hall, 1991 Upper Buford Circle, Saint Paul, MN 55108, USA
[b] Department of Horticulture, Colorado State University, 311 Shepardson Hall, Fort Collins, CO 80523, USA

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Abstract

High densities of antagonistic *Streptomyces* are associated with plant disease suppression in many soils. Here we review use of inoculation and organic matter amendments for enriching antagonistic *Streptomyces* populations to reduce plant disease and note that effective and consistent disease suppression in response to management has been elusive. We argue that shifting the focus of research from short-term disease suppression to the population ecology and evolutionary biology of antagonistic *Streptomyces* in soil will enhance prospects for effective management. A framework is presented for considering the impacts of short- and long-term management on competitive and coevolutionary dynamics among *Streptomyces* populations in relation to disease suppression.

Keywords: Inoculation; Biocontrol; Antagonist; Green manure; Organic amendment; Streptomyces

1. Introduction

1.1. *The genus* Streptomyces

Streptomyces is a genus of 500+ species of gram positive, filamentous bacteria in the Phylum Actinobacteria, Order Streptomycetales, Family Streptomycetaceae. *Streptomyces* are ubiquitous in soil habitats and aquatic sediments (Gontang et al., 2007). Among their most notable features is their capacity to produce an extraordinary diversity of antibiotics. *Streptomyces* have been estimated to produce up to 100,000 distinct antimicrobial compounds, of which only a small number have been identified to date (Watve et al., 2001). Antibiotic production is highly variable among individual *Streptomyces* (Davelos et al., 2004; Vetsigian et al., 2011), and most isolates produce multiple antibiotics (Challis and Hopwood, 2003). The diversity of secondary metabolite production among *Streptomyces* is due in part to genomic structure, with abundant transposable elements near the ends of the linear chromosome allowing for widespread movement and exchange of ‘accessory’ genes (Chen et al., 2002). Bioactive compounds from *Streptomyces* have important applications in human medicine as antibiotics, chemotherapeutants (Cragg et al., 2009), anti-obesity drugs (Weibel et al., 1987), immunosuppresents (Kim and Park, 2008), and blood pressure medications (Ihara et al., 1991). In nature, bioactive compounds are perceived to be crucial to *Streptomyces* life history in soil and in symbiotic associations, where antibiotics as weapons or as signaling molecules are believed to provide a competitive fitness advantage. As a group, *Streptomyces* are viewed predominantly as soil saprophytes with a crucial role in nutrient cycling (Kennedy, 1999), but they are also found as endophytes, as pathogens of plants and immunocompromised humans, and as beneficial symbionts with a wide variety of higher organisms, including insects, plants, and sponges (Dunne et al., 1998; Loria et al., 2007; Kaltenpoth et al., 2009; Khan et al., 2010; Hulcr et al., 2011).

* Corresponding author.
E-mail addresses: kinkel@umn.edu (L.L. Kinkel), schl0453@umn.edu (D. C. Schlatter), matt.g.bakker@gmail.com (M.G. Bakker), aren0058@umn.edu (B.E. Arenz).

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Most importantly for this review, inoculated and indigenous *Streptomyces* have also been widely recognized for their potential for controlling soilborne plant pathogens.

Here we review the history and current status of diverse approaches for managing *Streptomyces* to achieve disease suppression. Subsequently, we explore the use of a coevolutionary model (Kinkel et al., 2011) for identifying *Streptomyces* population and habitat characteristics most likely to influence the success of management practices in fostering disease-suppressive *Streptomyces* communities in soil. This approach distinguishes the short-term (ecological) effects of management on existing populations from longer-term (evolutionary) effects on species interactions. Finally, we emphasize the benefits of a shift in focus from immediate disease suppression to the population ecology and evolutionary biology of antagonistic *Streptomyces*. We propose that a longer-term perspective will enhance prospects for achieving consistent and effective disease suppression.

2. Disease suppression and *Streptomyces*

2.1. Background and history

Almost 100 years ago, Greig-Smith (1917) first noted the capacity of *Streptomyces* (which he referred to as *Actinomyces* or *Streptothrix*) to suppress other soil microbes. Subsequently, Millard (1923) reported that green manures, or crops grown specifically for biomass to be incorporated into soil, could reduce infection of potatoes by pathogenic *Actinomyces* (*Streptomyces*) *scabies*. Millard hypothesized that the significant food source provided by green manures precluded the organism from becoming pathogenic and causing potato scab. Sanford (1926) further investigated the mechanisms by which rye green manure reduced potato scab, and rejected the hypothesis that green manures work by reducing pathogen hunger stress. Instead, Sanford noted that *Actinomyces scabies* is "very sensitive to the secreted products of many molds and bacteria, some of which prevent its growth", and suggested green manures favored the antagonistic bacteria that inhibited the pathogen. Subsequently, Millard and Taylor (1927) took the final step in showing that inoculating soil with a saprophytic (non-pathogenic) *Actinomyces* isolate could significantly reduce both disease (potato scab) and pathogen populations. Millard and Taylor concluded that the saprophytic inoculated strain outcompetes the pathogen in soil, thereby reducing plant disease.

This short series of studies provided seminal evidence for the potential for naturally-occurring and inoculated *Streptomyces* to control plant pathogens in soil. These studies also fundamentally changed the way that plant pathologists thought about root diseases by highlighting the significant influences of microbial interactions within soil communities on plant disease development (Garrett, 1955). Finally, this work inspired and challenged researchers to develop management tools for exploiting the potential of *Streptomyces* populations to achieve disease control.

Over the past 80 years, researchers have built diligently upon the empirical foundation established by the work of Sanford, Millard, and colleagues. Research on *Streptomyces*-based disease suppression continues to be strongly focused on selection of antagonistic isolates for inoculation and on the use of green manures or nutrient amendments for enhancing antagonistic populations. However, a skeptic could argue that we have advanced little despite nearly a century of promise: research remains largely empirical, consistent disease control is elusive, and we lack an organizing framework for understanding or predicting effective disease suppression by *Streptomyces*.

Here we summarize briefly the status of research into *Streptomyces*-based disease suppression, focusing on inoculative biocontrol, exploration of naturally-suppressive soil communities and management of indigenous populations in soil. We propose a shift in emphasis from short-term management for suppressing plant disease towards longer-term management of species interactions and coevolutionary dynamics as a means for enriching *Streptomyces* densities, diversities and antagonistic activities in soil.

2.2. Inoculative biocontrol

Following Millard and Taylor's early work, many researchers explored the potential for *Streptomyces* to inhibit diverse plant pathogens, including *Helminthosporium*, *Ophiobolus* (*Gauemannomyces*), and others (Katznelson, 1940). Over the past 50 years, there has been extensive study of the mechanisms by which *Streptomyces* might inhibit pathogens in soil, including antibiosis, nutrient competition, production of degradative enzymes, nitrous oxide production, and quorum quenching (Mahadevan and Crawford, 1997; Mahmoudi et al., 2011; Cohen and Mazzola, 2006). Among these, antibiotic-mediated inhibition of pathogens is most often the primary focus suppression of plant diseases by *Streptomyces*. The diversity of secondary metabolites produced by *Streptomyces* offers tremendous potential for suppressing fungal, bacterial, oomycete, and nematode pathogens. Moreover, their broad capacities to metabolize diverse carbon and nitrogen sources enhances the potential for *Streptomyces* to effectively compete for resources in the rhizosphere (Schlatter et al., 2009). In addition to direct toxic effects on other microbes, nitrous oxide production by *Streptomyces* has been suggested to activate plant defenses, offering an additional novel means for protecting plants against pathogens (Cohen et al., 2005). More recently, *Streptomyces* have been shown to degrade the signaling compounds that coordinate gene expression required for pathogenicity in *Pectobacterium carotovorum*, suggesting a further mechanism for disease suppression (Mahmoudi et al., 2011). Finally, production of chitinases or plant growth-promoting compounds has been reported to contribute to disease suppression by some *Streptomyces* isolates (Quecine et al., 2008; El-Tarabily et al., 2000; Berg et al., 2001; Verma et al., 2011).

At present, *Streptomyces* spp. for biocontrol against bacterial, fungal, oomycete, viral, and nematode pathogens remain an active target for biocontrol research and many promising *Streptomyces* strains have been characterized, evaluated for efficacy, and, in some cases, patented (Yuan and Crawford, 1995; El-Tarabily et al., 2009; Bressan and Figueriredo, 2007; Meschke and Schrempf, 2010; Clermont et al., 2011; Esnard et al., 1995). A variety of *Streptomyces*-based products are available commercially for inoculation, including Mycostop (Verder Oy, Finland) and Actinovate (Natural Industries, Incorporated, USA), with additional products in the research and development pipeline.

Most efforts at inoculative biocontrol focus on selecting the most antagonistic *Streptomyces* isolate available and applying that isolate at the highest possible density onto seeds or into soil. Despite some successes with this approach, however, *Streptomyces*-based inoculative biocontrol remains inconsistent in field settings (Hiltunen et al., 2009; Leisso et al., 2009; Ryan et al., 2004), and in particular, colonization and growth of inoculated *Streptomyces* in soil remain unreliable (Katznelson, 1940; Weindling et al., 1950; Ryan and Kinkel, 1997). Although some studies have explored inoculum dose–response relationships and the effects of colonization success on biological control (Bressan and Figueiredo, 2007; Ryan and Kinkel, 1997), there is little comprehensive information on the correlates of successful colonization or on the relationships between soil or rhizosphere population densities and disease suppression for *Streptomyces*. Work by Johnson (1994) and Johnson and DiLeone (1999) provides a useful theoretical framework for exploring dose–response relationships, and suggests an asymptotic relationship between antagonist dose or density and plant disease. However, the effectiveness of antagonist densities in suppressing plant disease can also be constrained by the spatial and temporal dynamics of the pathogen and the antagonist populations (Kinkel et al., 2002; Johnson, 2010), so that antagonist density, while important, may be unlikely to provide a simple predictor of disease suppression.

The potential for endophytic *Streptomyces* to control plant disease has become a recent focus of research. *Streptomyces* are found commonly as endophytes in a wide variety of host plants (Sardi et al., 1992), and have been hypothesized to play a role in protecting plants against pathogens (Coombs and Franco, 2003; Lehr et al., 2008), to aid in nutrient uptake (Verma et al., 2011), to modify plant development (Tarkka et al., 2008), and to stimulate both mycorrhizal and rhizobial associations (Schrey et al., 2005; Tokala et al., 2002). While there is evidence that *Streptomyces* inoculated onto seeds can establish endophytic populations and reduce plant disease in some systems (Misk and Franco, 2011; Conn et al., 2008), the significance of *Streptomyces* endophytes to plant fitness remains relatively poorly understood (Conn and Franco, 2004). However, the protected endophytic habitat may minimize the challenge of achieving successful inoculant colonization, which has proven difficult in competitive soil communities. Further work exploring the relationships between soil *Streptomyces* populations, endophytic populations, and disease suppression is needed to determine the potential for endophytic *Streptomyces* to suppress plant disease.

2.3. Naturally-occurring disease suppressive soils

Streptomyces have been implicated in naturally-occurring and induced disease suppressive soils active against fungal (Weller et al., 2002; Hjort et al., 2010; Mendes et al., 2011), bacterial (Lorang et al., 1989; Meng et al., 2011; Rosenzweig et al., 2011), and nematode (Zuckerman et al., 1989) plant pathogens. Suppressive soils are notable for their capacity to provide high levels of disease suppression despite conditions conducive to disease or infection, and provide perhaps the best evidence that microbially-mediated disease suppression can be both highly effective and stable over long periods of time (Weller et al., 2002). However, in most cases the role of *Streptomyces* in disease suppression has been concluded based on relatively limited information on the presence of antagonistic populations in the suppressive soil (Lorang et al., 1989; Zuckerman et al., 1989). There has been little systematic consideration of the characteristics of *Streptomyces* communities associated with disease suppressive soils, although the broad assumption has been similar to inoculative biocontrol: better disease control results from higher densities of more inhibitory *Streptomyces* (Wiggins and Kinkel, 2005a, b).

Among the suppressive soils in which *Streptomyces* have been implicated, potato scab-suppressive soils have been the most well-studied. Long-term potato monoculture has been associated with the development of potato scab-suppressive soils in multiple locations (Menzies, 1959; Lorang et al., 1989; L. Wanner, personal communication; Meng et al., 2011). In Minnesota, *Streptomyces* communities were compared in a disease-suppressive and in an adjacent disease-conducive soil (Kinkel, unpublished). Total *Streptomyces* densities were measured for each soil, and a random collection of 50 saprophytic *Streptomyces* isolates from each soil were evaluated individually for their abilities to inhibit a collection of 21 plant pathogenic *Streptomyces scabies* isolates in vitro. These data document community-wide differences in saprophytic *Streptomyces* populations that may be crucial to disease suppression. First, *Streptomyces* densities were significantly greater in suppressive than in conducive soils (Fig. 1). Furthermore, both the frequency of antibiotic inhibition against pathogenic *S. scabies* and the intensity of inhibition were greater among isolates from the suppressive than from the conducive soil (Fig. 2). Finally, the diversity of antibiotic phenotypes (profile of inhibitory interactions across pathogen isolates) among antagonistic *Streptomyces* was greater for the suppressive than for the conducive communities (Shannon–Wiener diversity index of 2.56 for suppressive soil and 1.85 for conducive soil).

These suppressive soil data are consistent with the hypothesis that high densities of antagonistic *Streptomyces* contribute significantly to disease suppression. While higher *Streptomyces* densities and more antagonistic phenotypes in suppressive soils may have been anticipated by the early work of Sanford, Millard and Taylor, as well as by recent work in other systems (e.g. Wanner, 2007; Postma et al., 2010) the

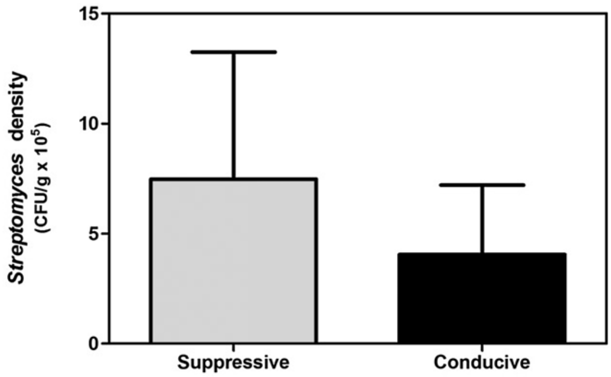

Fig. 1. *Streptomyces* population densities per g soil in disease-suppressive and conducive soils (mean ± SE; $n = 10$ replicate samples per soil; $F = 8.21$; $P < 0.01$).

finding of greater diversities in inhibitory phenotypes offers unique insight into the potential bases for stable, highly effective disease suppression. Specifically, diversity in inhibitory phenotypes is likely to offer a means for enhancing disease suppressive capacity of soil communities by increasing the numbers and variety of pathogens susceptible to inhibition, as well as reducing the likelihood of pathogen resistance to suppression. Synergy and contingency, or complementarity, among antibiotics have been suggested to be important drivers for the evolution of the extraordinary diversity of *Streptomyces* antibiotics (Challis and Hopwood, 2003), and should contribute to disease suppression. In total, these data are consistent with a significant role for competitive species interactions in the development of disease-suppressive *Streptomyces* communities in soil. More importantly, these data suggest a relatively straightforward model for the development of disease suppressive soil communities focusing on microbial competitive interactions and the effects of density- and frequency-dependent selection on soil populations (Fig. 3). Briefly, we hypothesize that:

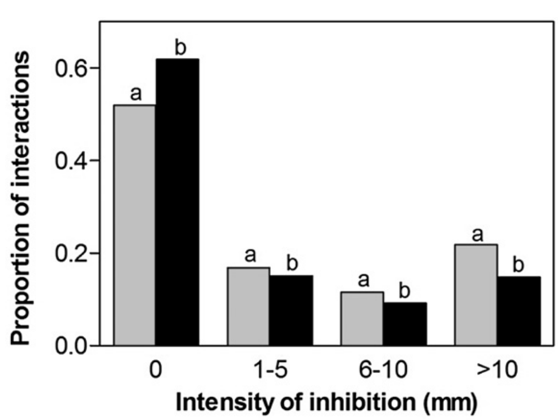

Fig. 2. Intensity of inhibition (inhibition zone sizes in mm) of pathogenic *S. scabies* by saprophytic *Streptomyces* from suppressive (gray bars) and conducive (black bars) soils. From a total of 1050 interactions per soil (50 saprophytic isolates × 21 pathogenic *S. scabies* isolates for each soil), bars quantify the proportion of interactions in each category. Differences between suppressive and conducive proportions within each category were analyzed using a chi-square test ($P < 0.05$).

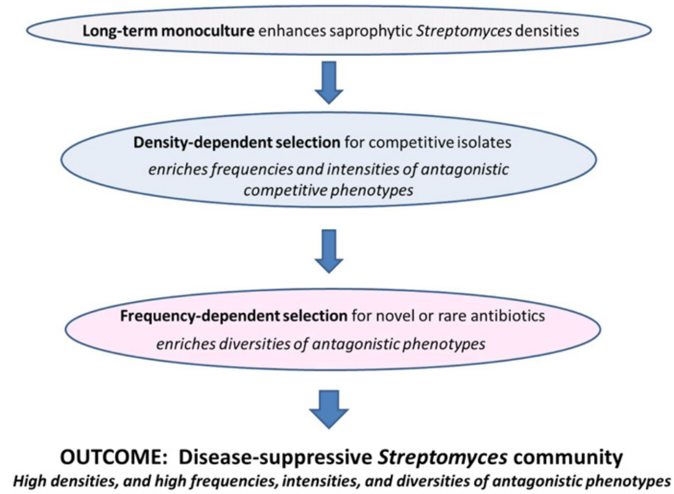

Fig. 3. A model for the development of naturally-occurring disease-suppressive *Streptomyces* communities following long-term potato monoculture.

1. Long-term potato monoculture enhances saprophytic *Streptomyces* densities.
2. Competitive interactions are both more frequent and more intense as population density increases in soil. Consequently, density-dependent selection will result in enrichments in the frequency and intensity of antagonistic competitive phenotypes within *Streptomyces* populations.
3. High densities and frequencies of antagonistic populations induce frequency-dependent selection for novel antagonistic phenotypes because novel or rare antibiotics confer relatively greater fitness benefits to the producer. Cumulatively, rare advantage will enhance the diversity of *Streptomyces* inhibitory phenotypes in highly antagonistic communities.
4. The outcome of sustained density- and frequency-dependent selection driven by competitive interactions within communities will be a highly diverse, antagonistic *Streptomyces* community with significant capacity to suppress plant pathogens. Specifically, soilborne plant pathogens, including many fungi, nematodes, and bacteria, including pathogenic *S. scabies*, are frequently highly sensitive to diverse antibiotics produced by saprophytic *Streptomyces*.

2.4. Active management of indigenous Streptomyces *populations: green manures, organic amendments, and induced disease suppression*

Green manures and other organic amendments have attracted interest both as a means of reducing pesticide inputs to the environment and of suppressing diseases for which pesticides are unavailable or plant resistance is lacking. Amendments can suppress pathogen populations directly, for example by production of isothiocyanates (Mazzola and Zhao, 2010) or nitrous oxides (Lazarovits et al., 2001), or indirectly, via shifts in soil microbial communities and their subsequent impacts on pathogens (Davis et al., 2010). We focus here on disease suppression mediated by shifts in *Streptomyces* communities in soil.

Streptomyces have been linked to the success of a variety of green manures, compost amendments, and integrated cropping systems in suppressing plant pathogens. In some cases, successful disease suppression following green manure treatments has been associated with enhanced *Streptomyces* densities. For example, incorporation of brassica green manures enhanced *Streptomyces* densities and reduced rates of apple seedling infection by the fungal pathogen *Rhizoctonia* (Mazzola and Zhao, 2010). Larkin et al. (2011a) evaluated the effectiveness of a variety of cropping systems for reducing potato diseases and found that the cropping system that offered the best disease control had higher estimated actinobacterial populations than a short-term continuous potato cropping system, although actinobacterial densities were not a simple predictor of disease suppression among fields. Shifts in *Streptomyces* phenotypes have also been reported in response to organic amendments (e.g. Cohen et al., 2005). Incorporation of brassica seed meal increased the proportions of antagonistic isolates and both the frequency and rate of nitric oxide production among isolates (Cohen et al., 2005). Other organic amendments and agricultural management practices have also been shown to increase *Streptomyces* densities or alter relative abundance (Ofek et al., 2009; Lenc et al., 2011). Because *Streptomyces* are frequent colonists of composted materials, compost amendments may influence soil *Streptomyces* communities by inoculation as well as by introduction of a food source (Inbar et al., 2005).

In Minnesota, green manures were explored as a means for controlling plant pathogens on potato, wheat, and alfalfa crops. Green manure crops were evaluated for both their effects on disease and on *Streptomyces* population densities and antagonistic phenotypes in soil. Green manures provided significant control of Verticillium wilt on potatoes and significantly enhanced alfalfa stand counts in *Phytophthora*-infested soil, but did not control *Fusarium* on wheat (Wiggins and Kinkel, 2005a, b; Perez et al., 2008). Densities of antagonistic *Streptomyces* post-green manure incorporation were significantly negatively correlated with scab disease on potatoes (Wiggins and Kinkel, 2005b), consistent with a significant role for antagonistic *Streptomyces* in disease suppression. Moreover, selection for antagonistic phenotypes in response to green manure treatments was a density-dependent phenomenon: the increase in *Streptomyces* antagonists in response to green manures was greater for higher density communities than for low density communities (Table 1; Fig. 3). Unfortunately, these studies did not track shifts in the diversity of antagonistic phenotypes in response to green manure treatments, and thus do not provide insight into the role of frequency-dependent selection in inducing disease-suppressive *Streptomyces* communities in response to management.

In total, there is broad evidence for the capacity of organic amendments to alter *Streptomyces* densities and antagonistic activities in soil, with significant potential for disease suppression. However, we have accomplished relatively little in advancing our fundamental understanding of the mechanisms by which *Streptomyces* populations are enriched in response to green manures, the population characteristics of *Streptomyces* communities in cases where green manures have provided successful disease suppression (but see Bernard et al., 2012 and Larkin et al., 2011a), or the microbial or soil factors that influence the capacity for green manure treatments to induce successful disease suppression.

Table 1
Relationships (Pearson correlation statistics, R, and associated *p*-values) between *Streptomyces* density prior to treatment and the change in the proportion of antagonists from pre- to post-green manure treatment (Wiggins and Kinkel, 2005b) Population densities and the proportion of *Streptomyces* antagonistic against each of four pathogens were determined before and after green manure treatment (July to October). Experimental details are described in Wiggins and Kinkel (2005b).

Treatment	Target pathogen			
	Streptomyces scabies	*Verticillium dahliae*	*Fusarium oxysporum*	*Rhizoctonia solani*
Green manure	$\mathbf{R = 0.39}$ ($P = 0.008$)	$\mathbf{R = 0.34}$ ($P = 0.02$)	$\mathbf{R = 0.32}$ ($P = 0.03$)	$\mathbf{R = 0.41}$ ($P = 0.006$)
Fallow	$\mathbf{R = 0.00}$ ($P = 1$)	$\mathbf{R = 0.41}$ ($P = 0.1$)	$\mathbf{R = 0.14}$ ($P = 0.6$)	$\mathbf{R = 0.07}$ ($P = 0.8$)

3. Rethinking the challenge of disease suppression

Over 80 years of research have documented an association of high densities of antagonistic *Streptomyces* with suppression of a diverse array of plant diseases. However, we have been unable to capitalize on this observation to achieve consistent disease control through active management of inoculated or indigenous *Streptomyces* populations. A major reason may be that we have framed the problem inappropriately. While research has focused on the challenge of suppressing plant disease, the challenge is more accurately conceived of as one of population ecology and evolutionary biology. If antagonistic *Streptomyces* populations suppress disease, then research must focus explicitly on identifying those factors that influence antagonist population dynamics in soil. Thus, progress will require systematic analysis of the short- (ecological) and longer-term (evolutionary) dynamics of antagonistic populations in response to management. Such analysis will benefit from development of a predictive framework that describes relationships between management strategies and *Streptomyces* community characteristics, and that allows for hypothesis testing and a deepened understanding of the dynamics of antagonist populations in soil.

A recently-proposed model for describing the coevolutionary dynamics of microbes in the development of disease-suppressive soils (Kinkel et al., 2011) provides a starting point for considering the specific influences of inoculation and organic amendments on *Streptomyces* community characteristics, including antagonist density, diversity and phenotypes in soil. The model focuses on the role of species interactions in *Streptomyces* population dynamics and hypothesizes that

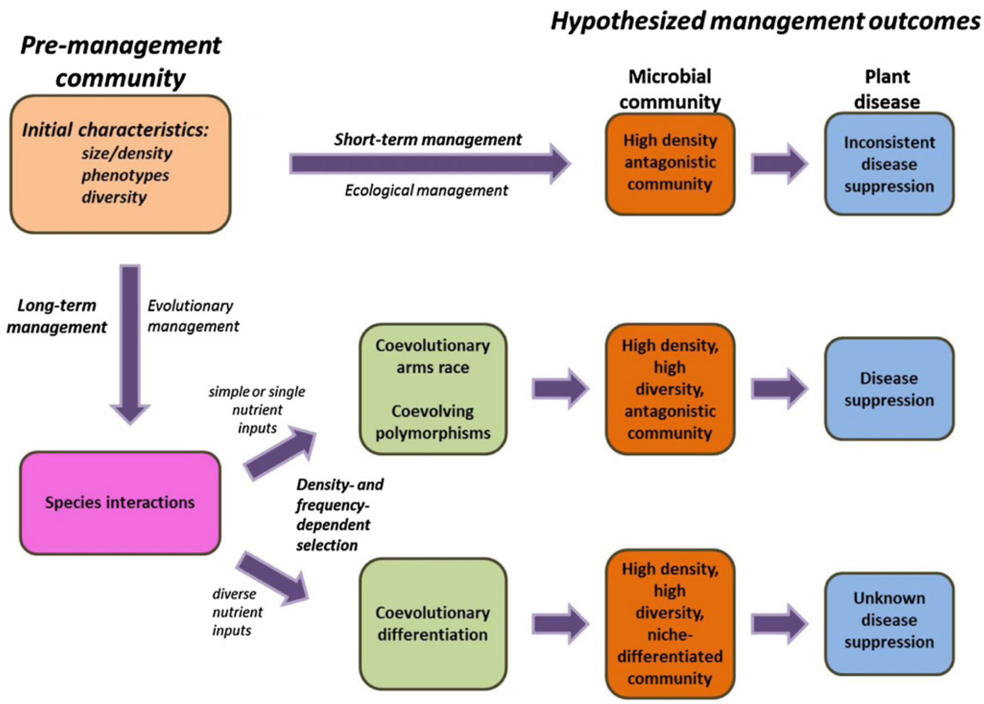

Fig. 4. A model for managing soil communities to enhance disease suppression. Short-term management focuses on rapid increases in *Streptomyces* densities or inhibitory activities via inoculation or organic amendments. Long-term management targets species interactions and coevolution, and seeks to generate high densities as well as high frequencies, intensities, and diversities of antagonistic phenotypes. Initial community characteristics are significant to both short- and long-term management outcomes.

competition and coevolution, or reciprocal selection and genetic change among coexisting *Streptomyces* populations, are crucial for the development of stable, highly disease-suppressive soil communities. We expand this model to identify microbial community characteristics that may be important predictors of the success of inoculative or organic amendment approaches to disease suppression. Practically, short-term management is a first step along a continuum to long-term management, but we distinguish these approaches here (Fig. 4; Table 2) to clarify the different potential outcomes and drivers of short-versus long-term success.

3.1. Short-term, ecological management

Most studies on management for disease suppression have focused on relatively short-term or immediate responses to management and seek to shift community antagonistic activity predominantly through inoculation or provision of a short-term food source. Yet the majority of studies provide limited or no information on the extent to which management was successful in inducing shifts in *Streptomyces* populations in soil (for exceptions see Larkin and Honeycutt, 2006; Mazzola and Zhao, 2010). More importantly, virtually no consideration has been given to the initial characteristics of the microbial community targeted for management. However, it is the initial community that is likely to determine the success or failure of management in achieving successful antagonist enrichment and, ultimately, disease suppression. For example, among inoculated *Streptomyces*, interactions with indigenous microbial populations are likely to be critical to the success of colonization and disease suppression (Fig. 4). This suggests that management success will be fundamentally influenced by initial community characteristics relevant to species interactions, including i) densities, which can index the likely frequency and intensity of interactions, ii) antagonistic and

Table 2
Observed and hypothesized advantages and disadvantages of short- vs. long-term management on *Streptomyces* populations and disease suppression.

Type of management	Short-term (ecological)	Long-term (evolutionary)
Target	Immediate increase in *Streptomyces* density and/or antagonistic phenotypes	Mediating species interactions to maximize the potential for a co-evolutionary arms race
Advantages	Inoculation offers precise control over antagonist characteristics Low cost and minimal time investments	Promotes diversity of antagonistic phenotypes; likely to enhance effectiveness, stability, and longevity of control Ongoing coevolution minimizes the likelihood of pathogen resistance Optimizes adaptation of suppressive populations to local habitat
Disadvantages	Poor predictability & reproducibility Potentially unstable; reliance on single isolates may select for pathogen resistance Highly localized effects (in cases of seed or rhizosphere inoculation)	Sustained investments (time, cost) may be required Time-to-effective control uncertain Trajectory toward niche differentiation may reduce antagonistic activities (but may offer an alternative mechanism for disease suppression?)

nutrient use phenotypes, which mediate species interactions, and iii) functional and phylogenetic diversity, which mediate evolutionary potential and niche utilization. In the case of inoculative biocontrol, for example, most attention has been given to identifying strains that are capable of suppressing a pathogen. However, successful inoculant colonization and disease suppression will also require an understanding of the nutrient or niche preferences of an inoculant relative to the indigenous community, the inoculant's potential for inhibition by indigenous *Streptomyces*, and its potential to inhibit indigenous antagonists. Indigenous *Streptomyces* diversity is also likely to be a significant negative predictor of success for establishment of novel inoculated populations in soil (e.g. van Elsas et al., 2012). In a similar fashion, initial community characteristics, and especially starting densities and nutrient use preferences of indigenous antagonistic *Streptomyces*, are also likely predictors of success of organic amendments (Wiggins and Kinkel, 2005a, b; Larkin et al., 2011b). Recognizing the significant role of species interactions in the short-term success or failure of management of *Streptomyces* populations highlights the significance of initial soil microbial community characteristics (densities, nutrient use preferences, diversities; e.g. Garrett, 1955) to success. Moreover, this approach helps to identify the characteristics of communities most conducive to short-term vs. longer-term antagonist enrichment by different management strategies (Fig. 4), offering the opportunity for optimized management for distinct locations.

3.2. Long-term, evolutionary management

Importantly, management also has significant longer-term impacts on microbial species interactions in soil, and indeed, we argue that these interactions should be a primary target of sustained agricultural management for disease suppression. For example, while effective short-term management may increase population densities of highly antagonistic *Streptomyces* phenotypes in soil, enhanced *Streptomyces* population densities or antagonistic activities over the long-term will impact species interactions and coevolutionary dynamics within soil communities. In fact, management to increase population densities may be more significant as a tool for long-term than short-term management because of the potential for coevolution among indigenous *Streptomyces* populations to generate diverse antagonistic phenotypes (Table 2; Figs. 3 and 4). A shift in focus from short- to long-term management suggests that both inoculation and organic matter amendments for managing *Streptomyces* communities should be deliberately reconsidered from the perspective of their impacts on species interactions and coevolutionary trajectories among *Streptomyces* populations in soil. For example, rather than viewing inoculation solely as an attempt to enrich densities of a single novel or highly inhibitory *Streptomyces* strain, inoculative strategies should aim to initiate or enhance an antagonistic coevolutionary arms race. This may require isolation of *Streptomyces* strains having very different characteristics from traditional biocontrol inoculants. For instance, it may be possible to develop multiple-strain inoculants with complementary properties to target both short- and longer-term prospects for sustained management of *Streptomyces* communities in soil (e.g. strong antagonists for short-term benefits, broad resource competitors with high carrying capacity but little inhibitory activity to jump-start coevolution for long-term impacts). Similarly, organic matter amendments should be considered not only based upon their potential for short-term 'pulses' of antagonist enrichment but also for their long-term capacity to impose ongoing selection for novel and strong antagonistic phenotypes within indigenous soil communities. Active management of species interactions shifts the focus from immediate disease suppression to longer-term correlates or indicators of antagonistic coevolutionary potential.

In considering a shift in focus towards long-term management of species interactions, it is important to note that there are multiple potential coevolutionary trajectories among interacting *Streptomyces* populations in soil (Fig. 4; Kinkel

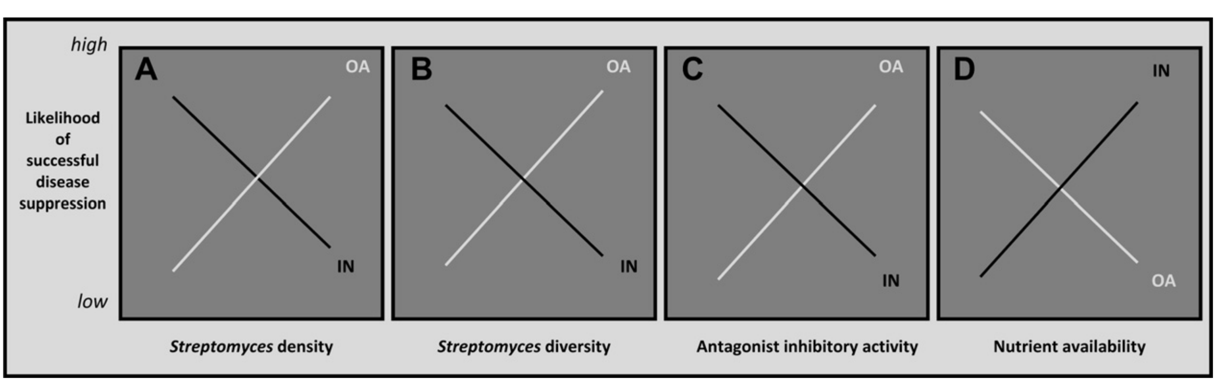

Fig. 5. Hypothesized effects of initial community and habitat characteristics on the potential for organic amendments (OA) or inoculated antagonistic *Streptomyces* (IN) to induce significant short-term shifts in *Streptomyces* densities or antagonistic activities in soil. For example, inoculative biocontrol is hypothesized to be less likely to be successful as indigenous population densities increase, while the effectiveness of organic amendments in inducing increases in antagonistic activity and disease suppression is hypothesized to increase with increasing initial indigenous population densities (though these relationships are unlikely to be as simple as the linear relationships described here). Communities having low potential for short-term success in response to management will require more sustained, evolutionary management to achieve disease suppression.

et al., 2011). In particular, the presence of multiple distinct nutrients within a habitat offers opportunities for niche specialization as an alternative to antagonism in response to competition (Schlatter et al., 2009; Kinkel et al., 2011). The resulting coevolutionary displacement among interacting populations may lead to niche differentiation over time (Thompson, 2005). Populations will coevolve to maximize their own fitness, but this suggests that habitat characteristics will be a crucial determinant of the coevolutionary trajectory and that our management of the habitat may be important for determining coevolutionary outcomes. Thus, for example, while simple or single nutrient soil amendments are likely to impose strong competition for a single limited resource and selection for antagonistic phenotypes, incorporation of complex or multiple nutrients into soil may result in an alternative trajectory of coevolutionary displacement. It is not clear whether a high diversity community of niche specialists has significant potential for suppressing soilborne plant pathogens. In fact, variation in the complexity of nutrients introduced into the soil among green manure or organic amendment treatments may be one significant contributor to the substantial variability in disease suppression achieved by different green manures (Hiddink et al., 2005; Kinkel et al., 2011). Overall, however, reframing the management objective towards long-term mediation of species interactions offers novel insights into strategies for achieving high density, high diversity, antagonistic *Streptomyces* communities in soil. In particular, this approach identifies community and habitat characteristics likely to have a significant impact on the effectiveness of management at altering *Streptomyces* communities (Fig. 5; Kinkel et al., 2011), and provides management targets that are likely to be important steppingstones to effective disease suppression (e.g. higher *Streptomyces* densities to enhance density-dependent selection, diverse populations to enhance evolutionary potential).

4. Summary

1. High densities of antagonistic *Streptomyces* are associated with disease suppression in many soil systems. However, despite decades of research we have been ineffective in developing consistent strategies for *Streptomyces* community management for effective disease suppression.
2. A shift in emphasis from immediate disease suppression to a focus on the population ecology and evolutionary biology of antagonistic *Streptomyces* in soil provides novel insights for enhancing management effectiveness. In particular, this shift highlights characteristics of soil microbial communities and habitats that are most conducive to success or failure of inoculation or organic amendments in achieving disease suppression (Figs. 4 and 5). In fact, habitats most conducive to short-term inoculant success may be least likely to exhibit successful disease suppression following organic matter inputs, and vice versa.
3. The effects of management on short-term population dynamics should be distinguished from management effects on long-term species interactions and coevolution within soil communities (Table 2). Management of coevolutionary species interactions extends the timeframes over which success or failure should be assessed, and suggests specific community characteristics that should be goals of long-term management as well as crucial correlates of progress towards a disease-suppressive *Streptomyces* community in soil.
4. Long-term management of evolutionary and coevolutionary dynamics has the potential to provide more stable and effective (better disease suppression, activity against a broad range of plant pathogens in diverse hosts) disease suppression than short-term ecological management because of its capacities to generate and sustain a high diversity of antagonistic phenotypes.

A comprehensive focus on the dynamics of antagonistic *Streptomyces* populations in soil and in response to diverse management strategies is needed to enhance our prospects for effective *Streptomyces*-mediated disease suppression. Emerging technologies that permit rapid phylogenetic and phenotypic analyses of microbial communities will be important for generating the data necessary for understanding the dynamics of antagonist populations and progress towards disease suppression (e.g. Mendes et al., 2011; Vetsigian et al., 2011; Rosenzweig et al., 2011). Such tools are also likely to deepen our understanding of the complex suite of genera that, in combination with the *Streptomyces*, contribute to plant disease suppression in soil, including *Bacillus*, *Pseudomonas*, *Trichoderma*, and the interactions among members of these genera. The focus on species interactions and coevolutionary dynamics considered here is broadly useful for evaluating interactions both within and among coexisting genera within the soil microbial community. A fundamental re-envisioning of the challenge of disease suppression as one of microbial population biology and evolutionary biology will enhance our understanding of *Streptomyces* and contribute significantly to achieving the promise of practical *Streptomyces*-mediated disease suppression conceived by Sanford and Millard nearly 100 years ago.

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