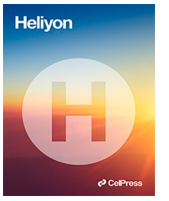
Heliyon 11 (2025) e42135

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Review article

Enhancing environmental decontamination and sustainable production through synergistic and complementary interactions of actinobacteria and fungi

Juliana M. Saez [a,b,1], Enzo E. Raimondo [a,c,1], Stefanie B. Costa-Gutierrez [a], Juan D. Aparicio [a,b], Domenica Mosca Angelucci [d], Enrica Donati [e], Marta A. Polti [a,b], Maria C. Tomei [d], Claudia S. Benimeli [a,f,*]

[a] Planta Piloto de Procesos Industriales Microbiológicos (PROIMI-CONICET), Avenida Belgrano y Pasaje Caseros, 4000, Tucumán, Argentina
[b] Facultad de Ciencias Naturales e Instituto Miguel Lillo, Universidad Nacional de Tucumán, Miguel Lillo 205, 4000, Tucumán, Argentina
[c] Facultad de Bioquímica, Química y Farmacia, Universidad Nacional de Tucumán, Ayacucho 491, 4000, Tucumán, Argentina
[d] Water Research Institute, National Research Council (CNR-IRSA), Via Salaria km 29.300, CP 10, Monterotondo Stazione, 00015, Rome, Italy
[e] Institute for Biological Systems, National Research Council (CNR-ISB), Via Salaria km 29.300, CP 10, Monterotondo Stazione, 00015, Rome, Italy
[f] Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Catamarca, Belgrano 300, 4700, Catamarca, Argentina

ARTICLE INFO

Keywords:
Actinobacteria
Fungi
Co-culture
Biotechnology
Bioremediation
Sustainable production

ABSTRACT

Actinobacteria and fungi are renowned for their metabolic diversity and adaptability to various environments, thus exhibiting significant potential for environmental decontamination and sustainable production. Both actinobacteria and fungi excel in producing diverse secondary metabolites and enzymes, offering valuable tools for industrial and environmental applications. Their ability to detoxify metals and degrade a wide range of organic pollutants, such as pesticides, hydrocarbons, and dyes, positions them as promising candidates for bioremediation.

Recent shifts in microbiological sciences emphasize research on mixed microbial populations. Microbial interactions in mixed communities emulate natural processes and yield emergent properties such as stability, robustness, and enhanced metabolism. Co-cultures of actinobacteria and fungi harness a broader range of genes and metabolic capabilities through their distinctive interactions, opening new avenues for developing novel products and/or technologies. This review provides a critical analysis of the present status of knowledge regarding the potential of actinobacteria-fungi co-cultures with a particular focus on novel functionalities and heightened production efficiency. These consortia are promising in several fields, from environmental applications to the biosynthesis of industrially relevant metabolites and enzymes, and enhancements in agricultural production. Although challenges still exist, their potential to address complex problems has been demonstrated and deserves further investigation.

1. Introduction

The members of the phylum Actinobacteria (recently renamed as Actinomycetota [1]) and fungi are recognized for their huge

* Corresponding author. PROIMI-CONICET, Avenida Belgrano y Pasaje Caseros, 4000, Tucumán, Argentina.
E-mail address: cbenimeli@yahoo.com.ar (C.S. Benimeli).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2025.e42135
Received 6 May 2024; Received in revised form 19 January 2025; Accepted 20 January 2025
Available online 20 January 2025

metabolic diversity and their ability to adapt to new hazardous environments and to colonize different substrates and niches, which is reflected in their cosmopolitan distribution [2,3]. They are important producers of diversified secondary metabolites, which have several applications in medicine, veterinary, and nutrition, such as antibiotics, anticancer, antiviral, enzyme inhibitors, immunosuppressors, nanoparticles, vitamins, and other biologically active compounds [4–9].

The potential of single cultures of fungi and actinobacteria for the biosynthesis of enzymes is widely documented; both microorganisms produce an extensive array of extracellular enzymes applied in industries and environmental bioremediation. Regarding the enzymes for industrial applications, some examples are α-amylase, with potential in the manufacture of beer, detergents, paper, and pharmaceuticals, among others; β-glucosidase, which could be applied in the food industries to enhance the flavor of fruit juice, tea, and wine [4,10,11], and ligninolytic enzymes which have great application in different sectors for composting, fermentation, biotransformation processes, and manufacturing of paper, among other products [6,12].

In natural habitats, actinobacteria and fungi play essential functions participating in carbon recycling and mobilization of essential bio-elements like nitrogen and phosphorus, which aids in soil fertility and the promotion of vegetation [2,13]. Also, some actinobacteria present characteristics typical of plant growth-promoting bacteria (PGPB) [14,15] and have been proven as effective biocontrol agents [16,17].

Concerning environmental applications, actinobacteria and fungi can degrade a broad range of organic compounds and detoxify inorganic pollutants, which makes them suitable agents for the bioremediation of various environmental compartments contaminated with of persistent inorganic and organic pollutants like heavy metals, pesticides, hydrocarbons, dyes, and other xenobiotics [7,18–21].

Currently, a "paradigm shift" is perceived in microbiological sciences, moving the focus from conventional monocultures toward research related to mixed microbial populations [22]. Interactions among the members in microbial mixed communities allow them to better approximate natural processes, by distributing the tasks among the populations, and reaching peculiar properties such as stability, robustness, and enhanced metabolism [23]. This can be explained because mixed cultures, composed of multiple microbial species, hold a wider range of genes and metabolic capabilities than pure cultures because of their capability to interact among them, thus enhancing their single features [18]. According to Liu and Kakeya [24], inter-kingdom co-culture offers a particularly intriguing approach to stimulate the secondary metabolism of both parties. Interactions between fungi and actinobacteria include both synergies or antagonism responses, which can be interesting in addressing complex challenges and developing new compounds or methods that can lead to advancements and improvements in different fields [22,25,26].

Despite the importance of the inter-kingdom co-cultures, there are currently few reviews in the literature concerning the application of mixed cultures of fungi and actinobacteria, and all of them are focused on the production of secondary metabolites. For instance, Liu and Kakeya [24] summarized important discoveries about chemical communication using secondary metabolites in co-culture systems. Also, Zhuang and Zhang [27] discussed the advances of utilizing cross-species co-cultures (including fungi-actinobacteria) for the finding of different natural compounds in the last few years, grouping them according to cultivation methods: liquid medium, solid medium, and special methods, highlighting for each method a few representative families of natural products, such as polyketides and alkaloids. Recently, Caudal et al. [28] reviewed the possibility of marine microorganisms' mixed cultures to improve the production of novel metabolites with pharmacological applications, reporting co-cultures of two bacterial strains, two fungal strains, and bacterial-fungal mixed cultures (including some cases with actinobacteria).

Also, unlike the above-mentioned approach, there are interesting recent reviews concerning the use of synthetic consortia and bacterial-fungal co-cultures for different applications such as environmental bioremediation, improvement of soil fertility, and agricultural productivity; however, none of them focuses on the use of actinobacteria in these co-cultures [14,18,29]. In this context, this review aims to describe the principal characteristics, ecology functions, crop benefits, and biotechnological uses of mixed cultures of microorganisms belonging to the actinobacteria phylum and fungi kingdom, as a strategy that mimics the natural living environment. Furthermore, it highlights and critically analyzes the potential of these interkingdom co-cultures for bioremediating polluted environments, developing smart agriculture with less environmental impact, and producing enzymes and bioactive molecules to implement a sustainable circular bioeconomy.

2. Single cultures vs. mixed cultures

The use of simple cultures in biotechnological processes carries several limitations. For instance, single cultures tend to have a narrower metabolic range compared to mixed cultures, so the products obtained could be limited. Also, single cultures may have slower metabolic rates, with longer production times and lower overall process efficiency. In addition, inefficient use of resources may occur, leading to waste and increased production costs [30]. Simple cultures are more susceptible to contamination by undesirable microorganisms, which can disrupt the production process and reduce yield and product purity. In addition, some species may exhibit genetic instability in single cultures, resulting in variations in product quality over time. Furthermore, monocultures can be more sensitive to changes in environmental conditions, such as pH, temperature, and oxygen levels, which can make process control more difficult.

In this sense, interactions between different species can produce a wider variety of products. In mixed cultures, different microorganisms can play complementary roles in nutrient utilization and product production and benefit from synergistic interactions between microorganisms, resulting in increased productivity and efficiency [12,31].

On the other hand, numerous genes responsible for biosynthesis remain unexpressed when microorganisms are cultivated under axenic conditions, thereby restricting the variety of microbial compounds attainable via fermentation in terms of chemical diversity. Conversely, the competition between two or more microorganisms in a co-culture may lead to enhanced production of constitutive compounds or even the production of cryptic compounds that are not distinguished in axenic cultures [32].

To address these drawbacks, mixed cultures are often used in biotechnological processes to take advantage of the diverse metabolic capabilities and interactions between different microorganisms, thereby improving process yields and product results. Even, intra-kingdom mixed cultures can also present difficulties related to lack of metabolic pathways or competition for nutrients. It is therefore relevant to perform interkingdom cultures, in an attempt to approximate the conditions under which they exist in nature, and their biotechnological potential is maximized [33].

Microbial interactions spanning across different biological kingdoms, including archaea, bacteria, fungi, and algae, offer valuable societal advantages within both natural and engineered environments. These advantages are typically unattainable when working solely with monocultures or consortia of microorganisms within the same kingdom. This disparity arises from the absence of mechanisms that facilitate symbiotic or competitive interactions in intrakingdom settings [34].

3. Isolation and formulation of actinobacteria-fungi co-culture

A microbial consortium, co-culture, or mixed culture is an association of two or more populations of microorganisms, acting together as a community in the same confined environment [35]. Two types of microbial consortia can be differentiated; one involves the assemble through the manual intervention of microorganisms (wild-type or genetically modified) with specific metabolic abilities for the formulation of defined (artificial or synthetic, respectively) consortia, whereas, on the other hand, natural or autochthonous microbial consortia, consist of naturally co-occurring microorganisms, obtained from a single source [36]. However, there is still a variety of expressions, showing a lack of consensus by specialists in the field [36]; in some cases, the terms defined, artificial, or synthetic are used indistinctly [23,29].

Defined microbial co-cultures based on mutualistic relationships have been commonly implemented to distribute their functions. Besides, these microbial co-cultures have several advantages such as preventing a nutritional deficiency due to the greater diversity of metabolic pathways present, the ability to exchange metabolites within the community, stability, and robustness within the microbial populations [23]. However, microbial species generally do not lead to a successful process when they are randomly combined into mixed culture. Thus, corresponding microbial strains should be selected considering their metabolic potential, focused on determined aspects of interest, such as the ability to metabolize specific compounds, eliminate contaminants, enhance plant yield, decrease virus harmfulness on host plants, produce a particular enzyme or metabolite, etc. Therefore, the selection of the strains is a key aspect for the design of defined mixed cultures, and hence, a careful study of each microbe should be performed first, testing *in vitro* and/or on-field applications, and then combining the microorganisms in a defined consortium to deal with the aforementioned aspects [29].

In the case of defined co-cultures involving actinobacteria and fungi, different types of interactions can occur among them, being antagonism a common phenomenon, mainly owing to the ability of actinobacteria to produce several secondary metabolites with antifungal activity [20,37]. For this reason, before formulating a defined mixed culture, the absence of direct antagonism between the members should be confirmed. In this sense, intending to design a co-culture of actinobacteria and fungi with the ability to remove lindane from different biomixtures, Saez et al. [37] first evaluated the presence of antagonism between four actinobacterial strains and three filamentous fungi, previously selected based on their individual degrading abilities. The antagonism evaluation consisted of facing the strains with each other in a rich agar medium and the subsequent macroscopic evaluation of the microbial development. The growth of the fungi *Trichoderma atroviride* S1EG1 and *Fusarium solani* S2EG3 was inhibited by the actinobacteria, which was evidenced as an inhibition halo, whereas no inhibitory effect was observed over *Trametes versicolor* S5NG1. Likewise, Sharma et al. [38] demonstrated the compatibility among *Streptomyces rochei* PAH-13, *Serratia marcescens* L-11, and *Phanerochaete chrysosporium* VV-18 since no inhibition was detected among them when they were grown together on nutrient agar medium plates, so these microorganisms were considered appropriate to design a defined co-culture for *in situ* bioremediation of soil contaminated by polycyclic aromatic hydrocarbons (PAHs).

The compatibility and co-existence between the members of the consortium are essential to achieve the survival of the members required for the successful application of the culture in a desired process; however, this does not necessarily guarantee a positive effect or enhanced efficiency regarding the pure cultures. For instance, Thion et al. [39] confirmed no growth inhibition between *Fusarium solani* MM1 and *Arthrobacter oxydans* MsHM11 suggesting no direct antagonism (*e.g.*, antibiotic production) between these model strains. Nevertheless, the PAH removal efficiency of the defined co-culture was significantly lower than the one obtained by the pure cultures of the strains involved; possibly microbial activities were indirectly affected by antagonistic interactions, such as pH modifications or competition for carbon sources between the two microorganisms, which conducted to fewer PAHs dissipation.

Besides compatibility, there are some other general recommendations to consider when preparing defined co-cultures involving two or more microorganisms such as actinobacteria and fungi that differ in terms of growth rates and their "aggressiveness" when cultured together under submerged conditions. In this sense, Boruta et al. [22] suggested that the inoculation strategy will depend on the goal of the process. For instance, if the aim is to stimulate the biosynthesis of a target metabolite produced by a faster-growing strain A, driven by or overproduced when a lower-growing strain B is present, the "equal chances" co-inoculation approach is suggested, either with spores or with the pre-culture of the organisms A and B together. The less aggressive strain, despite being dominated, is likely to maintain at least some activity and thus induce a cellular response in a dominant strain, such as the secondary metabolites production or the substrates utilization in co-culture. If, on the opposite, the focus is on the slower-growing strain, providing additional time for this microorganism to develop the biomass, strengthen its defenses against future microbial rivals, and stimulate its metabolic pathways before confronting it with a dominant, fast-growing microorganism, could be an effective approach [22].

On the other hand, autochthonous co-cultures could be a better alternative to mimic natural environments. Fungi and bacteria inhabit diverse environments and co-evolve, cooperate, and communicate with each other [40]. Many fungi and actinobacteria also

compete for environmental niches, and for that reason through millions of years of evolution, under certain conditions, they can be able to produce potent inhibitors to deal with potential competitors. In this sense, the autochtonous consortia could be found as good natural producers of antimicrobial compounds. For instance, Haggag and Abdall [41] isolated from grape leaves *Streptomyces aureofaciens* and *Rhodotorula glutinis* strains which demonstrated to be good candidates as biocontrol agents against the ochratoxin A (OTA)-producer *A. niger* in grapes, being the grapes' pollution and their by-products by OTA considered a big problem for the health risks related to the consumption of such products by human beings.

Other common sources for the isolation of natural microbial consortia are environmentally polluted samples since they are more likely to lead to potent co-cultures for bioremediation processes [42]. For this, suitable enrichment techniques and their improvement in the laboratory by various procedures, such as acclimation or directed evolution, are commonly used. To achieve robust, tolerant, and efficient consortia for bioremediation purposes, the selected microbial partners are cultured with different concentrations of the target pollutants with the expectation that the microorganisms will eventually display physiological or genetic changes to better deal with the surrounding conditions [18]. Fungi can be enriched together with actinobacteria using conventionally adopted enrichment procedures to obtain highly specialized aerobic consortia. Therefore, the presence of fungi in bacterial co-cultures previously achieved by applying the same technique cannot be excluded [43]. In this sense, Jacques et al. [44] isolated a fungal-bacterial consortium from soil samples belonging to a treatment plat of petrochemicals using an enrichment technique in which soil samples were first used to inoculate soil artificially contaminated with the target pollutant, anthracene 250 mg kg^{-1} and left for 176 days at room temperature. Then, 1 g of that was applied to inoculate a liquid mineral medium contaminated with 250 mg L^{-1} anthracene as the sole carbon and energy source, for higher enrichment of anthracene degraders. After three weekly enrichment transfers, the liquid culture was plated and colonies with different morphologies were continually streaked until purification. Six bacteria, including three actinobacteria, and one fungus, identified as *Fusarium oxysporum*, were isolated from the enrichment culture.

The application of specialized autochthonous mixed cultures involving actinobacteria and fungi isolated from polluted sites can provide higher and more reproducible contaminant degradation rates than those achievable with pure cultures or defined mixed cultures of degrading microorganisms [45]. This behavior is attributed to the ability of the members of enriched consortia to maintain their native ability to cooperate symbiotically with each other, which could contribute to the growth and activity of the microorganisms responsible for the final pollutant mineralization [44].

Recently, complex organic amendments, *e.g.* sludge, manure, or compost, have been proposed as sources of microbial consortia. These materials generally contain a high bacterial and fungal variety exhibiting genetic and metabolic diversity, in combination with several essential nutrients that can sustain the growth, survival, and colonization of allochthonous microorganisms in the inoculated site. However, these organic amendments could include pathogenic bacteria, such as *Listeria monocytogenes*, *Salmonella* spp., *Campylobacter coli* and *C. jejuni* [43], and their application in bioaugmentation strategies would entail environmental risks that need to be carefully evaluated.

4. Actinobacteria and fungi co-cultures for biotechnological applications

Microbial consortia are characterized by more properties than an individual microbial inoculum, due to the interactions of the microorganisms that populate them. The association among the members reflects synergistic or syntrophic lifestyles, in which the range of growth and nutrient flow is conducted more effectively than in individual populations [46]. Furthermore, competitive and antagonist interactions between species can exert positive outcomes in terms of promotion traits and metabolite production. Hence, the co-culture of fungi and bacteria, particularly actinobacteria, has been reported for multiple biotechnological applications. They have improved soil quality for sustainable agriculture, provide food security, and allow greater nutrient uptake and biocontrol of pathogens [14]. Besides, the co-cultivation of actinobacteria and fungi has been a successful approach to stimulate the synthesis of novel bioactive metabolites [32,47], enzymes [23], as well as being employed as bioremediation agents for organic and inorganic pollutants from diverse environmental matrices [48,49].

Notably, in the case of the application of these consortia under field conditions in natural settings, the success of microbial consortia will depend on several factors such as the type and function of strains, the environmental conditions (nutrients, climate, salinity, among others), and their persistence in nature after inoculation [50].

The use and integration of omics tools and advanced technologies could enable a comprehensive understanding of actinobacteria-fungi interactions. These insights can lead to the discovery of novel biotechnological applications and contribute to advancements in environmental remediation, agriculture, and natural product discovery [20,51–53]. Some of these technologies have been utilized to investigate different interactions, including those in microbiomes, plant-bacteria relationships, plant-endophytic fungi associations, and insect-microorganism interactions, among others [54–56]. However, studies specifically addressing actinobacteria-fungi interactions are currently lacking.

4.1. Bioremediation

A great variety of microorganisms is present in contaminated sites: fungi, protozoa, algae, and bacteria, the latter being the main degraders in bioremediation processes. Degrading fungi and actinobacteria are usually isolated from highly contaminated areas, under the premise that inhabiting these conditions, they could have developed the ability to synthesize enzymes capable of acting on different pollutants, and can therefore tolerate and degrade these toxic substances [57]. Although the isolation of microorganisms does not necessarily have to be performed from the contaminated site where they will be used for bioremediation, generally autochthonous microbial populations from soils without a contamination history have a reduced ability to metabolize pollutants [45].

The mineralization of complex organic pollutants usually involves the effective coexistence and involvement of different species with complementary substrate specificity. Generally, many bacteria can degrade low molecular weight (LMW) toxic compounds, while fungi can degrade high molecular weight (HMW) toxic compounds, through enzymatic activities and multiple cooperative pathways [45]. Thus, fungi and actinobacteria could be metabolically complementary during bioremediation processes. For example, the natural degradation of PAHs appears to be the result of sequential synergistic cooperation between fungi and bacteria, in which fungi perform the initial oxidation stage, transforming HMW and/or insoluble compounds into LMW and/or soluble intermediates, which may serve as easier degradable substrates for bacteria. This metabolic sequence is well documented in benzo(α)pyrene degradation [45,58]. Similarly, Byss et al. [59] demonstrated that the fungus *Pleurotus ostreatus* interacts positively and synergistically with actinobacteria for the detoxification of creosote-contaminated soils and, although actinobacteria are the main agents in the removal of hydrocarbons, the Ascomycota members perform also a crucial role during the degradation of recalcitrant oil-hydrocarbons. Moreover, fungal exudates are important carbon sources for bacteria, so they could stimulate bacterial growth, and consequently, increase pollutant degradation [60].

Besides, fungal hyphae could act as vectors for transporting actinobacteria, as demonstrated by Ellegaard-Jensen et al. [61] by using a system in which sand spiked with the herbicide was separated from the co-culture by a sterile glass beads layer. The actinobacterium *Arthrobacter globiformis* D47 was found in the top layer of the sand when the vials contained the consortium with the fungus *Mortierella* sp. LEJ702. This phenomenon is ideally useful in soils with low matric potentials and with unconnected water films, where bacterial spreading is reduced [62,63]. Besides, fungal hyphae in soils allow the formation of a water film in which bacterial degraders can move toward the pollutant [64].

In some cases, mixed microbial cultures with the physiological and metabolic features required for bioremediation may not co-exist in soils, particularly for those recently anthropogenically contaminated. In such cases, bioaugmentation of contaminated soils with consortia integrated by highly specialized actinobacterial and fungal strains is a promising option for a successful remediation process [65]. Owing to the metabolic versatility of these microorganisms, the application of actinobacteria-fungi co-cultures is attractive and offers the advantage of combining the degradative capabilities of different microorganisms to complete the degradation of parent compounds and their metabolites.

Table 1 presents some examples of co-cultures including actinobacteria and fungi used for the bioremediation, selected based on the different contaminated matrices and toxic compounds involved. A more extended list is presented in Supplementary material (S1). Jacques et al. [66] stated that the mineralization of a hydrocarbons mixture by autochthonous microorganisms in an artificially contaminated soil reached up to 20 %. However, when the soil was bioaugmented with a consortium formed by five bacteria, including an actinobacterium and one fungus isolated from a historically contaminated soil, the mixed culture mineralized between 96 % and 99 % depending on the hydrocarbon. Moreover, bioaugmentation of the soil with the co-culture resulted in a CO_2 production approximately 312 % higher than the one obtained with single bacteria or fungus inoculation. Similarly, Sharma et al. [38] informed that the dissipation of fluorene (75 %), anthracene (52.2 %), phenanthrene (67.8 %), and pyrene (39.2 %) in minimal medium after 7 days of incubation was higher in the broth inoculated with a microbial co-culture involving a bacterium (*Serratia marcescens* L-11), an actinobacterium (*Streptomyces rochei* PAH-13), and a fungi (*Phanerochaete chrysosporium* VV-18) than in the broth inoculated with the

Table 1
Selected examples of co-cultures involving actinobacteria and fungi employed for bioremediation of contaminated matrices.

Co-cultures	Pollutants	Contaminated matrices	Outcomes	References
Serratia marcescens L-11 + *Streptomyces rochei* PAH-13 + *Phanerochaete chrysosporium* VV-18	PAHs	Minimal medium (MM) and soil with 50 μg mL^{-1} or 50 μg g^{-1} of each PAH (fluorene, anthracene, phenanthrene, and pyrene)	MM: 75 %, 52.2 %, 67.8 %, and 39.2 % of degradation of fluorene, anthracene, phenanthrene, and pyrene, respectively, after 7 days Soil: 83.5–100 % of removal of PAHs after 30 days	[48]
Rhodococcus erythropolis + *Fusarium solani*	PAHS + VOCs	Air stream contaminated with formaldehyde, toluene, and benzo [α]pyrene (BaP)	Removal efficiencies in the steady state: 80 % for formaldehyde and BaP, and almost 100 % for toluene	[83]
Four *Streptomyces* sp. strains + *Trametes versicolor* SGNG1	Lindane	Biomixtures contaminated twice with lindane 2 g kg^{-1} at 0 and 66 days	80–87 % of removal after 60 days (1st contamination); 20–52 % of removal after 20 days (2nd contamination)	[47]
Micrococcus luteus + *Rhodococcus equi* + *Aspergillus niger*	Greywater	Residential wastewater with TOC: 385.90 mg L^{-1}, oil and grease: 58 mg L^{-1}	BOD removal: 454.5 mg L^{-1}, COD removal: 915.7 mg L^{-1}, oil and grease reduction: 48.09 mg L^{-1} in 96 h	[59]
Bacillus licheniformis KT986159.1 +*Bacillus* sp. KF956639.1 + *Gordonia amicalis* KM113029.1 + *Leifsonia* sp. KJ191763.1 + *Penicillium raperi* KC797647.1 + *Penicillium janthinellum* AY373921.1 + *Penicillium glabrum* LT558918.1 + *Trichoderma harzianum* LN714612.1	Zn	Soil artificially contaminated with Zn (250 and 1250 mg kg^{-1})	The bacteria-fungi consortium alleviated the adverse effects of Zn, however, it failed to reduce Zn bioavailability	[58]
Rhodococcus sp. D310-1 + *Enterobacter* sp. D310-5 + spent mushroom substrate of *Pleurotus eryngiu*	Chlorimuron-ethyl	Soil historically contaminated with chlorimuron-ethyl (19.2 mg kg^{-1})	93.1 % of removal after 80 days	[9]

single microorganisms (with removal percentages in the range of 4–28 %). This synergistic effect among the three microorganisms could be due to the ability of *Serratia marcescens* L-11 to produce catechol 1,2-dioxygenase and lipase, of *Streptomyces rochei* PAH-13 to produce a biosurfactant, and of *Phanerochaete chrysosporium* VV-18 to produce ligninolytic enzymes [67,68]. In the same direction, Wang et al. [45] designed three mixed cultures: one composed of four bacterial strains (including actinobacteria), one consisting of seven fungal strains, and one fungal-(actino)bacterial co-culture (all the strains), and tested their ability to remove HMW PAHs (phenanthrene, fluorene, and pyrene) from contaminated soil. The fungal-bacterial co-culture, which simulates the environment of real polluted sites, showed the maximum pyrene removal (67 %) in 28 days, compared to the bacterial (56 %) and fungal (39 %) mixed cultures. The same tendency was recorded during the fluorene and pyrene degradation, thus corroborating that microbial consortia including actinobacteria and fungi can be even more successful in degrading chemical contaminants than mixed cultures including only bacteria or fungi.

In bioremediation, favorable environmental conditions must be guaranteed to ensure adequate growth and microbial activities. In some situations, the addition of nutrients (carbon or nitrogen sources), micronutrients, water, and oxygen, could favor the growth of the microbial population, which in turn stimulates the activity of native and exogenous microorganisms, accelerating the pollutant removal rates. Thus, the biostimulation strategy is generally applied simultaneously with bioaugmentation to achieve greater pollutant degradation [65,69,70]. In this sense, some researchers evaluated the combined strategy of bioaugmentation with actinobacteria-fungi consortia and biostimulation to favor the degradation of PAHs in soils. Sharma et al. [38] demonstrated that the addition of three biostimulant agents (ammonium sulfate, compost, and paddy straw) enhanced PAHs degradation in soil by the fungal-bacterial-actinobacterial co-culture formed by *Phanerochaete chrysosporium* VV-18, *Streptomyces rochei* PAH-13, and *Serratia marcescens* L-11. Notably, the microbial consortium was successful in removing contaminants when three amendments were present, although the PAHs degradation was faster in the compost-amended soil. For their part, a microbial consortium was constructed by Lee et al. [71] taking into account their capability to degrade aliphatic hydrocarbons and their emulsifying activity. This consortium consisted of seven microbial strains, including two actinobacteria (*Micrococcus* sp. KSS-8 and *Rhodococcus* sp. KOS-1) and one fungus (*Yarrowia* sp. KSS-1). The application of this microbial consortium was successful in enhancing the clean-up of diesel fuel-polluted soil supplemented with nutrients (nitrogen and phosphorus) in laboratory- and bulk-scale experiments, suggesting it would be useful for cleaning up organic compounds in polluted environments.

Actinobacteria-fungi consortia also appear to be feasible for the treatment of air contaminated with PAHs and volatile organic compounds (VOCs), although the removal efficiency is influenced by different factors such as temperature and the pollutant chemical structure. In this context, Morales et al. [72] tested the ability of a consortium integrated by a fungus (*Fusarium solani*) and an actinobacterium (*Rhodococcus erythropolis*) to degrade indoor air pollutants [toluene, formaldehyde, and benzo[α]pyrene (BaP)] by calculating the degree of the pollutant mineralization as the CO_2 percent yield. As a result, for instance, for BaP, the highest CO_2 production rates were measured with the actinobacterial-fungal co-culture, regardless of temperature and pollutant concentration. Moreover, in the co-culture, the role of *F. solani* was dominant since the fungus would start the BaP degradation, leading to intermediate metabolites that can be subsequently more easily mineralized by the actinobacteria. Later, Vergara-Fernández et al. [73] evaluated the feasibility of this consortium for treating an air stream contaminated with the three pollutants in a biofiltration system, by estimating its performance under different experimental conditions. The biofiltration system bioaugmented with the co-culture presented high flexibility for the simultaneous abatement of the tested contaminants, with the removal efficiencies being high and largely independent of each other in a broad range of inlet loads. However, the removal efficiencies were reduced by decreasing the temperature of the biofiltration system.

Mixed cultures containing actinobacteria and fungi have also been demonstrated to degrade pesticides. For example, the consortium involving the fungus *Mortierella* sp. LEJ702, the bacterium *Variovorax* sp. SRS16, and the actinobacterium *Arthrobacter globiformis* D47 showed faster mineralization of ^{14}C-labelled diuron than the single cultures of the three tested strains, which mineralized less than 5 % of this compound. Remarkably, the three-member consortium mineralized 32.2 % in 54 days, and although it did not lead to the complete mineralization of diuron, the toxicity levels were reduced [61]. Similarly, a consortium composed of four actinobacteria and a fungus was designed for lindane removal in biomixture systems [37]. The actinobacteria *Streptomyces* sp. A2, A5, A11, and M7 were selected based on their ability to remove lindane [74], and the white rot fungus *Trametes versicolor* SGNG1 was selected because of its lignocellulolytic and laccase activities against different substrates, its ability to remove different organic pollutants [75], and the absence of direct antagonism effects with the actinobacteria. The co-culture was used to inoculate biomixtures formulated with sugarcane bagasse, peat, and different soil types, which were twice artificially contaminated with lindane 100 mg kg^{-1}, at days 0 and 66. According to the soil type, differences in lindane removal were found between the biomixtures. For the three soil types, pesticide removal rates were higher in the bioaugmented biomixtures than in non-bioaugmented ones after 60 days of inoculation. Furthermore, lindane half-life values in all bioaugmented biomixtures were lower than the ones detected in non-bioaugmented biomixtures during the first contamination. When biomixtures were recontaminated, only those constructed with silty loam soil and bioaugmented with the consortium showed a lower lindane half-life than the non-bioaugmented systems. In this sense, it could be worthy to re-inoculate the biomixtures with the consortium after recontamination to increase lindane dissipation. At a field scale, this action could be evaluated by growing the microorganisms in bioreactors using low-cost substrates, as it has been already evaluated for *Streptomyces* sp. A5 [76].

The immobilization of co-cultures on suitable carriers and their ability to be cryopreserved and stored at low temperatures for a long time are relevant factors to take into account when inoculating actinobacteria-fungi consortia into contaminated matrices. Zanaroli et al. [43] demonstrated the efficiency of hydrocarbon biodegradation and the stability of two fungal, bacterial, and actinobacterial consortia after cryopreservation and storage at −20 °C for six months, being interesting agents for the bioaugmentation of diesel fuel polluted sites. For their part, Wang et al. [77] informed that the pyrene dissipation by a bacterial-fungal co-culture

immobilized on farm byproducts was 59.6 % higher than the one obtained by the free co-culture. The use of a solid carrier for bioremediation protects microbial cells and enzymatic systems from harsh environmental conditions and reduces susceptibility to contamination by foreign microorganisms, by acting as a protective surface and creating a microhabitat that preserves the microorganisms. Besides, the abundant micropores present in the carrier materials allow excellent mass transfer of water, oxygen, nutrients, and hydrocarbons, as well as provide additional nutrients for microorganisms.

More recently, Zang et al. [26] combined an efficient chlorimuron-ethyl-degrading mixed culture composed of the bacterium *Enterobacter* sp. D310-5 and the actinobacterium *Rhodococcus* sp. D310-1, being spent mushroom substrate of *Pleurotus eryngiu* used as a carrier to evaluate its bioremediation ability. The inoculum immobilized degraded 93.1 % of chlorimuron-ethyl in soil historically contaminated at 80 days of the assay, while the soil inoculated with the free bacterial co-culture achieved a removal efficiency of 21.4 %. Notably, alterations in the autochthonous microbial structure were recorded in the first 80 days after bioaugmentation with the co-culture combined with the spent mushroom substrate. During this period, the abundance of *Enterobacter* and *Rhodococcus* genera increased while the abundance of other genera decreased. Nonetheless, the microbial population structure gradually recovered after 180 days, since it returned to the initial levels. This is remarkable because the applied strategy would have no significant long-term effect on the soil microbial structure.

Inorganic contaminants, for example, heavy metals, are non-degradable, hence, remediation of these compounds involves their conversion into less toxic forms or immobilization to reduce their bioavailability. In this context, an approach adopted to reduce heavy metal hazardous disposal in the environment is the application of co-cultures based on the synergetic effect of potentially robust metabolisms. Typically, fungal populations tend to accumulate heavy metals primarily, followed by releasing various metabolites like organic acids and siderophores, which cause the precipitation of these potentially harmful elements through a biosorption mechanism [29]. Therefore, consortia involving fungal and actinobacterial communities could result in the complete conversion and biosorption of heavy metals in a polluted environment. For example, a co-culture comprising a combination of bacteria (*Bacillus* sp., *E. coli*, *Pseudomonas* sp., *Salmonella* sp., and *Streptococci* sp.), fungi (*Aspergillus* sp., *Mucor* sp., *Penicillium* sp., and *Rhizopus* sp.) and actinobacteria (*Nocardia* sp., *Micrococcus* sp., *Micromonospora* sp., and *Rhodococcus* sp.) showed a bioremediation potential of Cd, Cu, and Fe (98.5, 99.6, and 100.0 %, respectively) in soils contaminated with heavy metals [78]. On the other hand, Strachel et al. [48] evaluated the result of the bioaugmentation of soil contaminated with Zn with a consortium consisting of four bacteria (including one actinobacterium) and four fungal strains. Unfortunately, the bioaugmentation failed to reduce Zn bioavailability in the soil, however, it minimized the adverse effects of Zn on the microbial diversity of the soil.

4.2. Sustainable agriculture

The applications of fungi-bacteria co-culture to sustainable agriculture aim at different approaches including improved nutrient uptake, reduction or elimination of external inputs, such as fertilizers or herbicides, and biocontrol of pathogens, pests, and diseases. All these practices pursue developing agroecology, ecological intensification of crops, and smart agriculture by taking advantage of soil ecological properties. Fungi-actinobacteria co-culture strategies targeted to smart agriculture include the exploitation of the relation established between actinobacteria, mycorrhiza, and plants. These mechanisms of interaction constitute a first step to design sustainable cropping systems, which rely on improved biodiversity of soils for the sustainable management of crop health, are shown in Table 2. Moreover, an additional case related to the symbiosis between actinobacteria, fungi, and ants, notably beneficial for agriculture purposes, is discussed.

4.2.1. Symbiosis between actinobacteria, mycorrhiza, and plants

The critical function of arbuscular mycorrhizal fungi (AMF) on agricultural sustainability for the stimulation of plant growth and

Table 2
Selected examples of co-cultures involving actinobacteria and fungi employed for sustainable agriculture.

Co-cultures	Crop	Operating conditions	Outcomes	References
Streptomyces coelicolor 2389 + *Glomus intraradices* LAP8	Sorghum (*Sorghum bicolor*)	Pot experiments: Sandy clay soil Incubation: 3 months at 20 °C, relative humidity 70 %, 16 h photoperiod and watered as needed with tap water	Co-inoculation led to positive effects on growth, nutrition and some metabolic activities of sorghum plants grown in soil amended with chitin waste of brawn scales	[89]
Streptomyces MCR9/ *Streptomyces* MCR26/ *Thermobifida* MCR24 + *Glomus mosseae*	*Trifolium repens* L.	Pot experiments: Soil-sand mix substrate. Incubation: 180 d in a growth chamber	Co-inoculation yielded higher plant growth and plant P acquisition, over those of the individual inoculants	[90]
Streptomyces sp. AcH 505 + *Piloderma croceum* (DSMZ 4824, ATCC MYA-4870)	*Quercus robur* L.	Petri dish with a 1:1 (v/v) mixture of fungal inoculum and gamma sterilized soil. *Streptomyces* sp. AcH 505 was inoculated at 3 and 7 weeks. Incubation: 8 weeks	*P. croceum* promoted AcH 505 growth in a culture system, however, in soil, the presence of oak microcuttings had significant effects on the interactions between both microorganims	[91]
Curtobacterium citreum BE + *Rhizophagus neocaledonicus* + *Claroideoglomus etunicatum*	Sedge (*Tetraria comosa*)	Mixture (4:1 v/v) of 2 mm sieved colluvial lateritic soil and commercial compost. Incubation: 8 months under greenhouse conditions watered every 2 days	Co-inoculation enhanced the dry weight of *T. comosa*, mineral nutrition, Ca/Mg ratio, and lowered metal translocation compared with the non-inoculated control	[8]

nutrient uptake (not only phosphorus and potassium but also other immobile nutrients, such as copper and zinc) of host plants is well documented [14]. In addition, various bacterial taxa coexist in symbiosis with AMF structures within diverse soil environments with possible benefits for both AMF and host plants. For instance, many actinobacterial species have been proven effective in developing symbiotic interactions with plants by colonizing their internal root tissues and promoting their growth by producing phytohormones, fixing N_2, and solubilizing inorganic phosphates. In this regard, a study conducted by Abdel-Fattah and Mohamedin [79] examined the impact of the symbiotic relationship between a vesicular-arbuscular mycorrhiza (*Glomus intraradices* no. LAP8) and chitin-decomposing *Streptomyces coelicolor* (strain 2389) on growth, nutrition, and metabolic functions of *Sorghum bicolor* plants cultivated in non-sterile soil enriched with chitin waste derived from brawn (*Penaeus japonicus*) scales. A substantial increase in the intensity of mycorrhizal root colonization and arbuscular formation was observed by inoculating the actinobacterium *S. coelicolor*. Moreover, although chitin treatment significantly reduced the levels of mycorrhizal root infection and led to higher chitinase activity, there was a marked increase in these levels with *S. coelicolor*.

In another study, Bourles et al. [25] assessed the influence of *Curtobacterium citreum* BE, derived from an ultramafic soil in New Caledonia, on the AMF symbiosis and growth of *Tetraria comosa*, a locally occurring sedge used in ecological restoration initiatives. They observed no significant effects on plant growth of two AMF species (*Rhizophagus neocaledonicus* and *Claroideoglomus etunicatum*) and *C. citreum* BE inoculated separately; on the contrary, their combined inoculation significantly improved the dry weight of *T. comosa* regarding the control without inoculation. Co-inoculated plants also presented enhanced mineral nutrition, an increased Ca/Mg ratio, and reduced metal translocation, which could be particularly useful for metal-contaminated soils.

The interaction between *Streptomyces* and AMF has also been investigated by Franco-Correa et al. [80]; they isolated thirty actinobacteria strains and analyzed them for key traits related to plant growth and mycorrhiza-helping activities. *Streptomyces* strains MCR9, MCR26, and a *Thermobifida* strain MCR24 were chosen to evaluate their interactions with AMF (*Glomus mosseae*) for their phosphate solubilizing/mineralizing and/or N_2-fixing capabilities. Co-inoculation of actinobacteria and *Glomus mosseae* showed synergic benefits on plant growth, and MCR9 and MCR24 sp. also on the uptake of phosphorus by plants. However, no effect of co-inoculation was observed regarding nitrogen acquisition, which was enhanced with either actinobacteria or AMF, alone or in combination.

Kurth et al. [81] performed a deep study to assess the effects of *Streptomyces* sp. AcH 505 and the ectomycorrhizal fungus *Piloderma croceum* on a host plant (*Q. robur*) and how the two microorganisms influence each other. For this, they conducted a systematic experimental design by growing AcH 505 and *P. croceum* as pure o mixed cultures in different culture conditions. The outcomes of their study indicate that the presence of microorganisms on plant roots positively affects the nature of actinobacterium-fungus interactions and that both microorganisms enhance the growth of the other one.

4.2.2. Symbiosis between actinobacteria, fungi, and ants

As mentioned for plant-fungi symbiosis, similarly, the mutualistic relationship among fungus-growing ants and their fungi serves as an example of relevant and beneficial symbiosis. Furthermore, various actinobacteria have developed a close association with multiple species of fungus-growing ants, with these bacteria possessing the ability to synthesize secondary metabolites that offer protection against diseases for both the ants and their fungal counterparts [82]. Indeed, usually, ants and their fungi rely on each other in a mutually dependent manner, thus maintaining stable fungal monocultures of utmost importance for the survival of both organisms, particularly when weeds or parasites are present [83]. To this aim, the occurrence of tripartite mutualism of actinobacteria-fungi-ants and their mutual effects are often under investigation. Beneficial outcomes for species involved in these symbiosis are documented for *Pseudonocardia* strains with the fungus *Leucoagaricus gongylophorus* and attine ant *Acromyrmex octospinosus* [84,85]. One theory to explain this, proposes that bacteria from the *Pseudonocardia* genus are the only mutual partners that have co-evolved with attine ants, and these microorganisms are passed vertically by the queens. In this connection, a recent study discovered an antifungal compound called dentigerumycin, produced by *Pseudonocardia*, in association with the lower attine ant *Apterostigma dentigerum*. This finding supports the idea that coevolved *Pseudonocardia* produces new antibiotics [84,85]. Another hypothesis is that attine ants collect actinobacteria from the soil, choosing and sustaining species that produce beneficial antibiotics. Consistent with this idea, *Streptomyces* strains isolated from *Acromyrmex octospinosus* have been also studied for their antagonist effect against the fungus *Escovopsis*, a virulent parasite of the attine fungal gardens [83].

4.3. Production of valuable metabolites

Secondary metabolites are naturally occurring compounds produced by organisms that are not required for basic viability but are essential for their survival strategies. These natural products are synthesized by plants, bacteria, fungi, and sponges and are inspiring modern drug molecules [28]. In particular, microorganisms of both terrestrial and marine origin are sources of bioactive compounds but the re-isolation of these substances is considered a challenge to be faced in the finding of novel natural products, for which, different approaches have been adopted. One of these is the co-culture system, which mimics the environmental conditions favoring the interactions between microorganisms [27]. This approach considers that inter- or intraspecies interactions predominate in nature and that the growth of a microorganism can modify or stimulate its metabolism when others are present. Conversely, this natural activation is missing in the monoculture developed under laboratory conditions and consequently, biosynthetic gene clusters are silent, resulting in a simplified metabolic profile [24]. Thus, the co-occurrence of different microbial populations in a complex system, allows the microorganisms to initiate chemical interactions and such biological stimuli result in the biosynthesis of diverse natural products by unlocking cryptic pathway expression [35].

Table 3 summarizes some interesting studies of actinobacteria and fungi co-cultures for the synthesis of valuable metabolites. A

wider list concerning the employment of fungal-actinobacterial co-cultures in this field is in Supplementary material (S2).

4.3.1. Actinobacteria – fungi co-culture for enhanced accumulation of known metabolites and production of novel natural products

The co-culture of different microbes simulating the natural state of the microbial community may conduce to the synthesis of secondary metabolites that appear as a result of representative events including chemical attack and protection, exploration of new chemical territories, competition for resources, defense against viral attacks, acts of predation and anti-predator, and reorganization of genetic material within chromosomes [35]. Also, some secondary metabolites may be produced by single cultures but their production can be up- or downregulated upon interspecies competition. It has been proven that fungal-actinobacterial interactions can lead to the specific activation of secondary metabolism genes in one or both microorganisms. For instance, Schroeckh et al. [86] reported that the co-cultivation of *Aspergillus nidulans* with the actinobacterium *Streptomyces rapamycinicus* induced the expression of the silent gene clusters in the fungusinvolved in the production of orsellinic acid and its derivatives. Further studies demonstrated that the bacterium induced the modification of the histone through the histone acetyltransferase (HAT) complex Saga/Ada in *A. nidulans* [87]. In more recent work, the new metabolite fumigermin has been identified in the fermentation produced by the mixed culture of *S. rapamycinicus* and *A. fumigatus* ATCC 46645. This fungal metabolite reversibly prevented the germination process in spores of *S. rapamycinicus*, which suggests that the fungus is induced by the actinobacterium to produce the fumigermin to protect its habitat resources and not to kill the bacterium [88]. In addition, the fungal co-culture with other *Streptomyces* spp. were tested and all of them induced the fumigermin biosynthesis but to a lesser extent than *S. rapamycinicus*. The authors also discovered that fumigermin biosynthesis was catalyzed by the partially reducing polyketide synthase FgnA.

Moussa et al. [89] examined the influence of *Streptomyces lividans* on secondary metabolite production by the fungus *Fusarium tricinctum*. Before adding the fungus, the actinobacteria were left for 72 h at 30 °C in flasks containing solid rice medium, to prevent the fungus from killing the bacteria, as in the case of the concurrent addition in the flasks. The mixed culture improved the synthesis of some known antibiotically active substances (i.e., lateropyrone, the depsipeptides enniatins B, B1, and A1, and fusaristatin A) also detected in the axenic fungal culture. This upregulated synthesis of antibiotic products may be interpreted as a chemical defense of the fungus. Moreover, the most interesting finding was several metabolites identified in the co-culture extracts that were not found in the fungal controls, such as zearalenone, (−)-citreoisocoumarin, macrocarpon C, and 7-hydroxy-2-(2-hydroxypropyl)-5-methylchromone, fusatricinones, and dihydrolateropyrone. However, the molecular patterns that underlie these specific fungal metabolic responses remained unraveled. Similarly, Yu et al. [90] discovered that novel antibacterial metabolites were produced by the co-cultivation of *Streptomyces rochei* MB037 and the fungus *Rhinocladiella similis* 35, as a response to the mutual competition for nutrition or space in the co-culture of these two strains.

In this line, Shi et al. [35] investigated the metabolic behavior of a consortium associated with a hydrothermal vent bacterial-fungal

Table 3
Selected examples of co-cultures involving actinobacteria and fungi employed for the production of valuable metabolites.

Co-cultures	Cultivation methods	Metabolites	Outcomes	References
Rhodococcus sp. RKHC-26/ *Gordonia* sp. PNM-25 + *Purpureocillium* sp. PNM-67	Solid medium using 4 different culture: LB + glucose, PDA, ISP2, and ISP3 (distance and contact assays)	Red dye	Co-culture induces red pigmentation in the fungus in response to a change in its metabolic production	[103]
Streptomyces lividans + *Fusarium tricinctum*	Mixed fermentation on solid rice medium	Lateropyrone, enniatins B, B1, and A1, fusaristatin A, fusatricinones A–D, dihydrolateropyrone, zearalenone, (−)-citreoisocoumarin, macrocarpon C, 7-hydroxy-2-(2-hydroxypropyl)-5-methylchromone	Co-culture led to the production of new compounds and enhanced the accumulation of known metabolites	[99]
Streptomyces rochei MB037 + *Rhinocladiella similis* 35	Cultivation in ISP2 medium with shaking for 11 days	The fatty acids borrelidins J and K, 7-methoxy-2,3-dimethylchromone-4-one, borrelidin, borrelidin F	Co-culture induces the production of polyketides with antibacterial activities against methicillin-resistant *Staphylococcus aureus*	[100]
Streptomyces rimosus ATCC 10970 + *Aspergillus terreus* ATCC 20542	Nine cultivation runs in a stirred tank bioreactor (5.5 L) with different co-culture initiation approach, medium composition, and pH	40 secondary metabolites	*S. rimosus* showed a tendency to dominate over *A. terreus*. Despite that, *A. terreus* had an influence on the production of secondary metabolites	[5]
Streptomyces sp. WU20 + *Aspergillus sclerotiorum* DX9	Cultivation under rocking conditions in PDB-LB liquid culture medium for 14 days at 28 °C	Notoamides R, X, I, F, and A	The fungi used the cyclo(Pro-Trp), produced by the actinobacteria, as the biosynthetic precursors of notoamides	[45]
Streptomyces avermitillis ATCC 31,267/ *S. coelicolor* A3(2)/ *S. griseorubens* DSM 40,160 + *Aspergillus niger* DSM 1957	Culture medium M3 supplemented with dry wheat bran (5 g L^{-1})	Metabolites such as terpenes, NRPS, siderophores, T1PKS, and lassopeptides	Depending on the co-cultures, an over-expression of secondary metabolite production were observed	[6]

community, consisting of *Streptomyces* sp. WU20 and *Aspergillus sclerotiorum* DX9. The co-culture improved the production of five alkaloids compared to the monocultures, namely notoamides R, X, I, and F, and stephacidin A. Furthermore, it was proven that the enhanced production of notoamides was due to the cyclodipeptide cyclo(Pro-Trp), also known as brevianamide F, which is a prominent component of the metabolome produced by *Streptomyces*, leading to the hypothesis that notoamide metabolites induction in the co-culture may be a result of the biotransformation of cyclo(Pro-Trp) by fungi.

4.3.2. Effects of the interaction between actinobacteria and fungi on the secondary metabolites production

The contact degree among the microorganisms may influence the secondary metabolites production since the variation in the metabolic profile could be due to either interactions resulting from physical contact or diffusible compounds secreted by one of the members of the co-culture acting as triggers of the silent biosynthetic pathways on the other/s [86]. Several authors have investigated the complexity of these interactions. For instance, Wu et al. [91] reported that a bacterial cell-free filtrate obtained from *Streptomyces coelicolor* A3 M145 culture was sufficient to stimulate the synthesis of phenylacetic acid and cyclo(Phe-Phe) by *Aspergillus niger* N402. This finding demonstrated that the phenylalanine metabolism change in the fungi was induced by secreted compounds acting as starter molecules or as elicitors of silent biosynthetic pathways, rather than by cell-to-cell contact with or nutrient depletion by *S. coelicolor*. On the opposite, Yu et al. [92] evidenced that the physical contact between *Aspergillus flavipes* CGMCC 3.15449 and *Streptomyces* sp. CGMCC4.7185 was necessary for inducing the cytochalasans production. The co-cultivation enabled the production of novel cytochalasans, notably five aspochalasins, and rosellichalasin, compared to their respective monocultures. Further studies highlighted that all the identified cytochalasans avoided the growth of their competitor *Streptomyces* sp., which means that they could have a potential ecological role.

Martínez-Buitrago et al. [93] carried out a screening of binary interactions between 14 different bacteria alongside the fungal isolate *Purpureocillium* sp. PNM-67, in solid media. All the co-cultures were firstly examined in a distance assay to highlight chemically mediated interactions and then, the co-cultures showing a phenotypic change, were also studied in a contact assay to evidence interactions due to cell-cell contact. They demonstrated that seven co-cultures induced the metabolic profile to change, five of them in consequence of diffusible compounds and the others as a result of physical contact. Notably, only the co-cultures of fungus and actinobacteria *Gordonia* sp. PNM-25 or *Rhodococcus* sp. RKHC-26 caused pigmentation of red color in the *Purpureocillium* sp. PNM-67 after the modification in the metabolic production.

4.3.3. Actinobacteria – fungi co-cultivation in bioreactors

An unusual practice for evaluating secondary metabolite production was utilized by Boruta et al. [22]. They co-cultivated an actinobacterium-fungus system, composed of *Streptomyces rimosus* ATCC 10970 and *Aspergillus terreus* ATCC 20542, in a stirred tank bioreactor. Unlike other studies, this work aimed at characterizing co-cultivation as concerning the secondary metabolic profiles as well as the bioprocess kinetics. The experimental set-up included nine cultivation runs, each one consisting of three-stirred tank

Table 4
Selected examples of co-cultures involving actinobacteria and fungi employed for enzyme production.

Co-cultures	Enzyme	Co-culture operating conditions	Outcomes	References
Streptomyces coelicolor 2389 + *Glomus intraradices* LAP8	Chitinase	Pot experiments: Sandy clay soil Incubation: 3 months at 20 °C, relative humidity 70 %, 16 h photoperiod and watered as needed with tap water	Chitin amendment resulted in an increase in the chitinase activity in soils co-inoculated	[89]
Streptomyces olivaceoviridis + *Aspergillus proliferans*	Exochitinase ChiO1	Co-cultivation at 30 °C without shaking (to avoid pellet formation)	Co-cultivation produced: (i) stimulation of the germination of *S. olivaceoviridis* spores, (ii) initiation of the outgrowth of some fungal spores to which the *S. olivaceoviridis* chitinase ChiO1 adheres, (iii) massive extension of viable networks of *S. olivaceoviridis* hyphae at the expense of fungal hyphae, and (iv) balanced proliferation of closely interacting fungal and *S. olivaceoviridis* hyphae	[105]
Streptomyces sp. F-6/F-7 + *Pleurotus ostreatus G5*	Lignin peroxidase, manganese peroxidase, and laccase	A 2 % v/v spore suspension of actinomycetes and 0.5 cm^2 of the mycelia of *P. ostreatus* G5 were mixed and maintained at 30 °C and 150 rpm for 12 days	The combined actinobacterium–fungus system decomposed alkali lignin effectively	[108]
Streptomyces rapamycinicus + *Aspergillus fumigatus*	Polyketide synthase	The co-culture was incubated at 37 °C	Co-cultivation induced a previously silent polyketide synthase pathway in the human pathogenic fungus *A. fumigatus*, and this led to the discovery of a previously unreported prenylated polyketide	[106]
Streptomyces avermitillis ATCC 31,267/*S. coelicolor* A3(2)/*S. griseorubens* DSM 40,160 + *Aspergillus niger* DSM 1957	Lignocellulolytic Carbohydrate Active enzyme (CAZyme)	Culture medium M3 supplemented with dry wheat bran (5 g L^{-1})	Metabolic diversity and CAZyme content increased with co-culture. Depending on the co-cultures, an over-expression of some enzymatic activities (xylanase, glucosidase, arabinosidase) were observed	[6]

bioreactors operating in parallel, one of them containing the co-culture whereas the others were the respective monocultures. The study revealed that the mixed culture of *A. terreus* and *S. rimosus* in a bioreactor promoted the formation of over 40 metabolites. The differences between the co-culture and the monocultures, regarding the secondary metabolites production, depended on both the growth medium composition and the strategy of co-culture initiation. In particular, it was evident that the choice of the co-cultivation strategy is strictly associated with the metabolic profile to be achieved. In this sense, Ścigaczewska et al. [94] highlighted that the microbial morphology depended on the initiation strategy applied for the co-cultivation. The simultaneous introduction of both microorganism pre-cultures resulted in the dominance of *S. rimosus* over *A. terreus*. Conversely, *A. terreus* dominated only when bacteria were introduced in the bioreactor after fungi. Moreover, the morphologically dominant microorganism in the co-cultivation was also metabolically prevailing.

4.4. Production of enzymes

Enzyme production or increased enzymatic activity is another positive outcome of co-cultures of fungi-actinobacteria, which, as for secondary metabolites, act as a biorefinery by stimulating their metabolic potential and by triggering molecule biosynthesis to implement a sustainable circular bioeconomy. The increase in enzyme production as a result of co-cultivation may be due to enzymatic synergy related to a greater diversity of enzymes. This condition offers a more effective degradation of the substrate, and/or growth synergy, i.e. a chemical interaction (interaction molecules, elicitors, secondary metabolites), as well as the sharing of metabolic pathways allows emulation of microbial development [23]. Examples of actinobacteria-fungi co-culture strategies providing an increase in metabolic activities have been mentioned in previous sections devoted to sustainable agriculture [25,80], bioremediation [26,49], and secondary metabolite production [88,90]. Further studies, mostly focused on enzyme activity are shown in Table 4.

Siemieniewicz and Schrempf [95] demonstrated the intimate actinobacterial-fungal interaction by co-culturing the highly chitinolytic *Streptomyces olivaceoviridis* and the ascomycete *Aspergillus proliferans*. No germination was detected in monocultures, while co-culturing provides (i) enhanced germination of spores of *S. olivaceoviridis*, (ii) initiation of the development of certain fungal spores for which bacterial chitinase ChiO1 attaches, (iii) substantial expansion of viable networks of bacterial hyphae by utilizing fungal counterparts as a resource, and (iv) balanced proliferation of closely interacting fungal and *S. olivaceoviridis* hyphae. The most interesting result is that the chitinase ChiO1 produced by *S. olivaceoviridis* was primarily observed bound to the fungal spores, suggesting their intimate interactions. The authors repeated the experiments of co-culturing by replacing *S. olivaceoviridis* with a chromosomal disruption mutant, lacking chitin-binding protein production but still actively releasing the chitinase ChiO1, and they observed each spore type germination, with delayed growth of both partners, followed by preferential proliferation of the fungus.

In general, both fungi and actinobacteria are endowed with a huge biosynthetic potential for enzyme production [96,97], however, most of those pathway genes can be silent or expressed at very low levels in the absence of specific triggers and/or physiological conditions. The induction of the expression of those silent biosynthetic pathways can be achieved in several ways including the mimicry of possible scenarios occurring in the habitat through co-cultivation with other species. For instance, König et al. [96] co-cultured the fungus *Aspergillus fumigatus*, a human pathogen, with the soil-derived actinobacteria *Streptomyces rapamycinicus*, to induce the silent polyketide synthase (PKS) pathway in *A. fumigatus*. Co-cultivation activated the PKS gene cluster encoding for an uncommon prenylated polyphenol (fumicycline A), giving evidence that the co-cultured actinobacterium modulates the regulation of the gene expression in *A. fumigatus*. Similarly, Detain et al. [23] performed monocultures involving a single fungal strain (*A. niger* DSM 1957) and co-cultures of it with one of three distinct *Streptomyces* strains, i.e. *S. avermitillis* ATCC 31,267, *S. coelicolor* A3(2), and *S. griseorubens* DSM 40,160, to achieve an efficient and rapid lignocellulose degradation. *Streptomyces* strains can exhibit diverse interactions, and due to their large enzymatic arsenal, they can provide lignocellulolytic Carbohydrate Active enZyme (CAZyme). In particular, through comparative genomics analysis of the strain *A. niger* DSM 1957 it was discovered that it harbored the maximum of several enzymatic classes included in CAZyme, such as ancillary activities, carbohydrate-binding module, carbohydrate esterases, and glycoside hydrolases. The authors found that some co-cultures exhibited heightened levels of certain enzyme activities (xylanase, glucosidase, arabinosidase) in comparison to the monocultures, indicating a distinctive form of microbial communication influenced by the specific microbial collaborator.

To promote biodegradation and biotransformation of lignin, two *Streptomyces* strains (F-6 and F-7) were isolated from forest soils (Dalian, China) and co-cultured with white-rot fungus (*Pleurotus ostreatus* G5) by Yang et al. [98]. Three different types of potentially lignolytic enzymes including manganese peroxidase (MnP), lignin peroxidase (LiP), and laccase were found in *P. ostreatus*, while both *Streptomyces* spp. strains had certain MnP activities, laccase activity of F-6 was observed at a high level, and LiP activity was not detected in the bacterial strains. The authors concluded that the *Pleurotus–Streptomyces* system can effectively degrade alkali lignin and may maintain degradation activity under non-sterile conditions, and the absence of LiP activity can be due to the stimulation of other enzymes, such as endoglucanase and xylanase, involved in lignin degradation.

5. Conclusions: Challenges and future research directions

Fungal-actinobacterial mixed cultures offer a broad range of promising applications in multifaceted fields. Restoration of soil health, disease prevention, crop productivity improvement, and sustainable production of biotechnological-based products such as modern drugs and industrial-interest enzymes, are just a small part of the wide range of potential uses of these co-cultures. This kind of inter-kingdom consortia has demonstrated increased resistance to fluctuating environmental conditions and the ability to enhance the metabolism of both parties either by improving the metabolic pathways available and/or by unlocking cryptic pathway expression, allowing a closer emulation of microbial communities in real scenarios. Sustainable development within the framework of a circular

economy provides a comprehensive approach to achieving long-term ecological balance, economic growth, and social equity. By prioritizing resource efficiency, waste reduction, and the regeneration of natural systems, this integrated model supports a more resilient and sustainable future. Thus, the application of actinobacterial-fungal co-cultures could have a positive impact on the eco-friendly remediation of contaminated environments. Additionally, the interaction mechanisms among these microorganisms enable the development of sustainable cropping systems that provide enhanced soil biodiversity for the effective management of crop health and open a new path for sustainable development in the frame of a circular economy.

However, there are still challenges to face when constructing and maintaining co-culture systems. The successful establishment of these consortia depends on several factors: the first one relies on the selection of the microbial strains and insurance of their growth compatibility. Then, the optimization of the culture media and conditions along with the sequence of inoculation should be thoroughly examined, since the growth requirements and rates could differ among members of the consortia. These parameters will be determinants for the survival and stability of all the microbial partners since one could prevail over the other/s.

Although there is still little knowledge of the dynamics and specific mechanisms of the interactions of fungal-actinobacterial populations, it is notable that in many cases, direct contact between the involved microorganisms is necessary to observe the activation of certain pathways, while in other cases it is mediated by molecules/plants/other species acting as signals/vectors/hosts. In this sense, a deeper understanding of the molecular and biochemical pathways is needed to get better benefits from these co-cultures.

Other major challenges of fungal-actinobacterial consortia inoculation are biotic interactions and competition with the autochthonous microbial community when working under real environmental conditions. Thus, it is necessary to study strategies to ensure the stability and performance of the co-cultures in real environments over time.

The actinobacteria-fungi co-culture strategy still faces the challenge of developing standardized protocols, as well as establishing methodologies to evaluate a large number of interactions simultaneously. Therefore, the selection of appropriate microbial mixed cultures for large-scale production still pushes for further research, to be fully exploited.

CRediT authorship contribution statement

Juliana M. Saez: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Conceptualization. **Enzo E. Raimondo:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Stefanie B. Costa-Gutierrez:** Writing – review & editing, Writing – original draft, Methodology. **Juan D. Aparicio:** Writing – review & editing, Data curation. **Domenica Mosca Angelucci:** Writing – review & editing, Data curation. **Enrica Donati:** Writing – review & editing, Data curation. **Marta A. Polti:** Writing – review & editing, Funding acquisition. **Maria C. Tomei:** Writing – review & editing, Conceptualization. **Claudia S. Benimeli:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Statements and declarations

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was supported by Agencia Nacional de Promoción Científica y Tecnológica (PICT 2020-02005, PICT-2021-CAT-I-00024, PICT 2021-0983, PICT 2021-00213), Consiglio Nazionale delle Ricerche and Consejo Nacional de Investigaciones Científicas y Técnicas (CNR-CONICET 2020-0117), Consejo de Investigaciones de la Universidad Nacional de Tucumán (PIUNT G739), and Consejo Nacional de Investigaciones Científicas y Técnicas (PIP 2020–2670, PIBAA 2021-0058, PIBAA 2021-1053).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2025.e42135.

References

[1] A. Oren, G.M. Garrity, Valid publication of the names of forty-two phyla of prokaryotes, Int. J. Syst. Evol. Microbiol. 71 (2021), https://doi.org/10.1099/ijsem.0.005056.

[2] A. Dornburg, J.P. Townsend, Z. Wang, Maximizing Power in Phylogenetics and Phylogenomics: A Perspective Illuminated by Fungal Big Data, first ed., Elsevier Inc., 2017 https://doi.org/10.1016/bs.adgen.2017.09.007.

[3] G.R. Lewin, C. Carlos, M.G. Chevrette, H.A. Horn, B.R. McDonald, R.J. Stankey, B.G. Fox, C.R. Currie, Evolution and ecology of Actinobacteria and their bioenergy applications, Annu. Rev. Microbiol. 70 (2016) 235–254, https://doi.org/10.1146/annurev-micro-102215-095748.

[4] F. Xie, W. Pathom-aree, Actinobacteria from desert: diversity and biotechnological applications, Front. Microbiol. 12 (2021), https://doi.org/10.3389/fmicb.2021.765531.

[5] M.G. Roth, N.M. Westrick, T.T. Baldwin, Fungal biotechnology: from yesterday to tomorrow, Front. Fungal Biol. 4 (2023) 1–11, https://doi.org/10.3389/ffunb.2023.1135263.

[6] V. Meyer, E.Y. Basenko, J.P. Benz, G.H. Braus, M.X. Caddick, M. Csukai, R.P. De Vries, D. Endy, J.C. Frisvad, N.G. Cimerman, T. Haarmann, Y. Hadar, K. Hansen, R.I. Johnson, N.P. Keller, Growing a circular economy with fungal biotechnology: a white paper, Fungal Biol. Biotechnol. (2020) 1–23, https://doi.org/10.1186/s40694-020-00095-z.

[7] A.G.T. Niego, C. Lambert, P. Mortimer, N. Thongklang, S. Rapior, M. Grosse, H. Schrey, E. Charria-Girón, A. Walker, K.D. Hyde, M. Stadler, The Contribution of Fungi to the Global Economy, Springer Netherlands, 2023, https://doi.org/10.1007/s13225-023-00520-9.

[8] U.D. Butt, S. Khan, X. Liu, A. Sharma, X. Zhang, B. Wu, Present status, limitations, and prospects of using *Streptomyces* bacteria as a potential probiotic agent in aquaculture, Probiotics Antimicrob, Proteins 16 (2024) 426–442, https://doi.org/10.1007/s12602-023-10053-x.

[9] N. Bano, D. Iqbal, A. Al Othaim, M. Kamal, H.M. Albadrani, N.A. Algehainy, H. Alyenbaawi, F. Alghofaili, M. Amir, Roohi, Antibacterial efficacy of synthesized silver nanoparticles of *Microbacterium proteolyticum* LA2(R) and *Streptomyces rochei* LA2(O) against biofilm forming meningitis causing microbes, Sci. Rep. 13 (2023) 1–14, https://doi.org/10.1038/s41598-023-30215-9.

[10] A. Ranjani, D. Dhanasekaran, P.M. Gopinath, An Introduction to Actinobacteria, Basics Biotechnol, Appl., 2016, pp. 3–38. http://www.intechopen.com/books/actinobacteria-basics-and-biotechnological-applications/an-introduction-to-actinobacteria.

[11] S.A. Sooklal, C. De Koning, D. Brady, K. Rumbold, Identification and characterisation of a fluorinase from *Actinopolyspora mzabensis*, Protein Expr. Purif. 166 (2020) 105508, https://doi.org/10.1016/j.pep.2019.105508.

[12] J. Wang, L. Li, H. Xu, Y. Zhang, Y. Liu, F. Zhang, G. Shen, L. Yan, W. Wang, H. Tang, H. Qiu, J.-D. Gu, Weidong Wang, Construction of a fungal consortium for effective degradation of rice straw lignin and potential application in bio-pulping, Bioresour. Technol. 344 (2022) 126168, https://doi.org/10.1016/j.biortech.2021.126168.

[13] A.A. Bhatti, S. Haq, R.A. Bhat, Actinomycetes benefaction role in soil and plant health, Microb. Pathog. 111 (2017) 458–467, https://doi.org/10.1016/j.micpath.2017.09.036.

[14] A. Aguilar-Paredes, G. Valdés, M. Nuti, Ecosystem functions of microbial consortia in sustainable agriculture, Agronomy 10 (2020) 1–19, https://doi.org/10.3390/agronomy10121902.

[15] G.C.M. Giaccio, J.M. Saez, M.C. Estévez, B. Salinas, R.A. Corral, E. De Gerónimo, V. Aparicio, A. Álvarez, Developing a glyphosate-bioremediation strategy using plants and actinobacteria: potential improvement of a riparian environment, J. Hazard Mater. 446 (2023), https://doi.org/10.1016/j.jhazmat.2022.130675.

[16] M. Ebrahimi-Zarandi, R. Saberi Riseh, M.T. Tarkka, Actinobacteria as effective biocontrol agents against plant pathogens, an overview on their role in eliciting plant defense, Microorganisms 10 (2022), https://doi.org/10.3390/microorganisms10091739.

[17] M. Kaari, R. Manikkam, K.K. Annamalai, J. Joseph, Actinobacteria as a source of biofertilizer/biocontrol agents for bio-organic agriculture, J. Appl. Microbiol. 134 (2023) 1–16, https://doi.org/10.1093/jambio/lxac047.

[18] E.J. Espinosa-Ortiz, E.R. Rene, R. Gerlach, Potential use of fungal-bacterial co-cultures for the removal of organic pollutants, Crit. Rev. Biotechnol. 42 (2022) 361–383, https://doi.org/10.1080/07388551.2021.1940831.

[19] U. Kües, Fungal enzymes for environmental management, Curr. Opin. Biotechnol. 33 (2015) 268–278, https://doi.org/10.1016/j.copbio.2015.03.006.

[20] A. Alvarez, J.M. Saez, J.S. Davila Costa, V.L. Colin, M.S. Fuentes, S.A. Cuozzo, C.S. Benimeli, M.A. Polti, M.J. Amoroso, Actinobacteria: current research and perspectives for bioremediation of pesticides and heavy metals, Chemosphere 166 (2017) 41–62, https://doi.org/10.1016/j.chemosphere.2016.09.070.

[21] N. Romano-Armada, M.F. Yañez-yazlle, V.P. Irazusta, V.B. Rajal, N.B. Moraga, Potential of bioremediation and PGP traits in *Streptomyces* as strategies for bio-reclamation of salt-affected soils for agriculture, Pathogens 9 (2020) 1–30, https://doi.org/10.3390/pathogens9020117.

[22] T. Boruta, A. Ścigaczewska, M. Bizukojć, "Microbial wars" in a stirred tank bioreactor: investigating the co-cultures of *Streptomyces rimosus* and *Aspergillus terreus*, filamentous microorganisms equipped with a rich arsenal of secondary metabolites, Front. Bioeng. Biotechnol. 9 (2021) 713639, https://doi.org/10.3389/fbioe.2021.713639.

[23] J. Detain, C. Rémond, C.M. Rodrigues, D. Harakat, L. Besaury, Co-elicitation of lignocelluloytic enzymatic activities and metabolites production in an *Aspergillus-Streptomyces* co-culture during lignocellulose fractionation, Curr. Res. Microb. Sci. 3 (2022), https://doi.org/10.1016/j.crmicr.2022.100108.

[24] C. Liu, H. Kakeya, Cryptic chemical communication: secondary metabolic responses revealed by microbial co-culture, Chem. Asian J. 15 (2020) 327–337, https://doi.org/10.1002/asia.201901505.

[25] A. Bourles, L. Guentas, C. Charvis, S. Gensous, C. Majorel, T. Crossay, Y. Cavaloc, V. Burtet-Sarramegna, P. Jourand, H. Amir, Co-inoculation with a bacterium and arbuscular mycorrhizal fungi improves root colonization, plant mineral nutrition, and plant growth of a Cyperaceae plant in an ultramafic soil, Mycorrhiza 30 (2020) 121–131, https://doi.org/10.1007/s00572-019-00929-8.

[26] H. Zang, W. Liu, Y. Cheng, H. Wang, X. An, S. Sun, Y. Wang, N. Hou, C. Cui, C. Li, Bioremediation of historically chlorimuron-ethyl- contaminated soil by co-culture chlorimuron- ethyl-degrading bacteria combined with the spent mushroom substrate, Microorganisms 8 (2020) 1–15, https://doi.org/10.3390/microorganisms8030369.

[27] L. Zhuang, H. Zhang, Utilizing cross-species co-cultures for discovery of novel natural products, Curr. Opin. Biotechnol. 69 (2021) 252–262, https://doi.org/10.1016/j.copbio.2021.01.023.

[28] F. Caudal, N. Tapissier-Bontemps, R.A. Edrada-Ebel, Impact of co-culture on the metabolism of marine microorganisms, Mar. Drugs 20 (2022), https://doi.org/10.3390/md20020153.

[29] P. Chaudhary, M. Xu, L. Ahamad, A. Chaudhary, G. Kumar, B.S. Adeleke, K.K. Verma, D.M. Hu, I. Širić, P. Kumar, S.M. Popescu, S. Abou Fayssal, Application of synthetic consortia for improvement of soil fertility, pollution remediation, and agricultural productivity: a review, Agronomy 13 (2023), https://doi.org/10.3390/agronomy13030643.

[30] T. Cui, B. Yuan, H. Guo, H. Tian, W. Wang, Y. Ma, C. Li, Q. Fei, Enhanced lignin biodegradation by consortium of white rot fungi: microbial synergistic effects and product mapping, Biotechnol. Biofuels 14 (2021) 1–11, https://doi.org/10.1186/s13068-021-02011-y.

[31] F. Kuhar, V. Castiglia, L. Levin, Enhancement of laccase production and malachite green decolorization by co-culturing *Ganoderma lucidum* and *Trametes versicolor* in solid-state fermentation, Int. Biodeterior. Biodegrad. 104 (2015) 238–243, https://doi.org/10.1016/j.ibiod.2015.06.017.

[32] J. Wakefield, H.M. Hassan, M. Jaspars, R. Ebel, M.E. Rateb, Dual induction of new microbial secondary metabolites by fungal bacterial co-cultivation, Front. Microbiol. 8 (2017) 1–10, https://doi.org/10.3389/fmicb.2017.01284.

[33] A.M.M. Mawad, A. El-Latif Hesham, N.M.H. Yousef, A.A.M. Shoreit, N. Gathergood, V.K. Gupta, Role of bacterial-fungal consortium for enhancement in the degradation of industrial dyes, Curr. Genom. 21 (2020) 283–294, https://doi.org/10.2174/1389202921999200505082901.

[34] S. Zhang, N. Merino, A. Okamoto, P. Gedalanga, Interkingdom microbial consortia mechanisms to guide biotechnological applications, Microb. Biotechnol. 11 (2018) 833–847, https://doi.org/10.1111/1751-7915.13300.

[35] Y. Shi, Y. Ma, J. Wei, Y. Ge, W. Jiang, S. He, X. Wu, X. Zhang, Comparative metabolomics reveals fungal conversion of co-existing bacterial metabolites within a synthetic *Aspergillus-Streptomyces* community, Mar. Drugs 19 (2021) 526.

[36] F. Massot, N. Bernard, L.M.M. Alvarez, M.M. Martorell, W.P. Mac Cormack, L.A.M. Ruberto, Microbial associations for bioremediation. What does "microbial consortia" mean? Appl. Microbiol. Biotechnol. 106 (2022) 2283–2297, https://doi.org/10.1007/s00253-022-11864-8.

[37] J.M. Saez, A.L. Bigliardo, E.E. Raimondo, G.E. Briceño, M.A. Polti, C.S. Benimeli, Lindane dissipation in a biomixture: effect of soil properties and bioaugmentation, Ecotoxicol. Environ. Saf. 156 (2018) 97–105, https://doi.org/10.1016/j.ecoenv.2018.03.011.

[38] A. Sharma, S.B. Singh, R. Sharma, P. Chaudhary, A.K. Pandey, R. Ansari, V. Vasudevan, A. Arora, S. Singh, S. Saha, L. Nain, Enhanced biodegradation of PAHs by microbial consortium with different amendment and their fate in in-situ condition, J. Environ. Manag. 181 (2016) 728–736, https://doi.org/10.1016/j.jenvman.2016.08.024.

[39] C. Thion, A. Cébron, T. Beguiristain, C. Leyval, PAH biotransformation and sorption by *Fusarium solani* and *Arthrobacter oxydans* isolated from a polluted soil in axenic cultures and mixed co-cultures, Int. Biodeterior. Biodegrad. 68 (2012) 28–35, https://doi.org/10.1016/j.ibiod.2011.10.012.

[40] K.N. Laland, N.J. Boogert, Niche construction, co-evolution and biodiversity, Ecol. Econ. 69 (2010) 731–736, https://doi.org/10.1016/j.ecolecon.2008.11.014.
[41] W.M. Haggag, A.M. Abdall, Evaluation of *Streptomyces aureofaciens* and *Rhodotorula glutinis* against ochratoxin A producing *Aspergillus niger* in grapevines, J. Microbiol. Res. 2 (2012) 170–175, https://doi.org/10.5923/j.microbiology.20120206.03.
[42] C.D. Elcey, A.A.M. Kunhi, Substantially enhanced degradation of hexachlorocyclohexane isomers by a microbial consortium on acclimation, J. Agric. Food Chem. 58 (2010) 1046–1054, https://doi.org/10.1021/jf9038259.
[43] G. Zanaroli, S. Di Toro, D. Todaro, G.C. Varese, A. Bertolotto, F. Fava, Characterization of two diesel fuel degrading microbial consortia enriched from a non acclimated, complex source of microorganisms, Microb. Cell Factories 9 (2010) 1–13, https://doi.org/10.1186/1475-2859-9-10.
[44] R.J.S. Jacques, B.C. Okeke, F.M. Bento, M.C.R. Peralba, F.A.O. Camargo, Characterization of a polycyclic aromatic hydrocarbon-degrading microbial consortium from a petrochemical sludge landfarming site, Ann. Finance 11 (2007) 1–11, https://doi.org/10.1080/10889860601185822.
[45] S. Wang, N. Nomura, T. Nakajima, H. Uchiyama, Case study of the relationship between fungi and bacteria associated with high-molecular-weight polycyclic aromatic hydrocarbon degradation, J. Biosci. Bioeng. 113 (2012) 624–630, https://doi.org/10.1016/j.jbiosc.2012.01.005.
[46] J.S. Hero, J.H. Pisa, N.I. Perotti, C.M. Romero, M.A. Martínez, Endoglucanase and xylanase production by *Bacillus* sp. AR03 in co-culture glycosyl hydrolases by *Bacillus* sp. AR03 in co-culture, Prep. Biochem. Biotechnol. (2017) 1–8.
[47] W. Ebrahim, M. El-Neketi, L.I. Lewald, R.S. Orfali, W. Lin, N. Rehberg, R. Kalscheuer, G. Daletos, P. Proksch, Metabolites from the fungal endophyte *Aspergillus austroafricanus* in axenic culture and in fungal-bacterial mixed cultures, J. Nat. Prod. 79 (2016) 914–922, https://doi.org/10.1021/acs.jnatprod.5b00975.
[48] R. Strachel, J. Wyszkowska, M. Baćmaga, Bioaugmentation of soil contaminated with Zinc, Water Air Soil Pollut. 231 (2020), https://doi.org/10.1007/s11270-020-04814-5.
[49] N. Rajpal, N. Divya, S. Sharma, K.J. Balasubramani, J.K. Ratan, Treatment of greywater using consortium of *Micrococcus luteus, Rhodococcus equi* and *Aspergillus niger*, J. Indian Chem. Soc. 97 (2020) 478–482.
[50] G. Santoyo, P. Guzmán-Guzmán, F.I. Parra-Cota, S. de los Santos-Villalobos, M.D.C. Orozco-Mosqueda, B.R. Glick, Plant growth stimulation by microbial consortia, Agronomy 11 (2021) 1–24, https://doi.org/10.3390/agronomy11020219.
[51] A.K. Passari, S. Sánchez, Actinobacteria: recent trends in genomics, omics study and discovery of novel natural products, Front. Microbiol. 12 (2021) 799737, https://doi.org/10.3389/FMICB.2021.799737/BIBTEX.
[52] Z. Wang, A. Gudibanda, U. Ugwuowo, F. Trail, J.P. Townsend, Using evolutionary genomics, transcriptomics, and systems biology to reveal gene networks underlying fungal development, Fungal Biol. Rev. 32 (2018) 249–264, https://doi.org/10.1016/J.FBR.2018.02.001.
[53] C.S. De Sousa, S.S. Hassan, A.C. Pinto, W.M. Silva, S.S. De Almeida, S. De Castro Soares, M.S.P. Azevedo, C.S. Rocha, D. Barh, V. Azevedo, Microbial omics: applications in biotechnology, Omi. Technol. Bio-Engineering Vol. 2 Towar. Improv. Qual. Life. (2018) 3–20, https://doi.org/10.1016/B978-0-12-815870-8.00001-2.
[54] A. Salvioli, P. Bonfante, Systems biology and "omics" tools: a cooperation for next-generation mycorrhizal studies, Plant Sci. 203–204 (2013) 107–114, https://doi.org/10.1016/J.PLANTSCI.2013.01.001.
[55] M. Srivastava, N. Malviya, T. Dandekar, Application of biotechnology and bioinformatics tools in plant–fungus interactions, Plant Biol. Biotechnol. Vol. II Plant Genomics Biotechnol. (2015) 49–64, https://doi.org/10.1007/978-81-322-2283-5_3.
[56] A. Malacrinò, Meta-omics tools in the world of insect-microorganism interactions, Biology 7 (2018) 50, https://doi.org/10.3390/BIOLOGY7040050.
[57] N.J. Pino, M.C. Dominguez, G.A. Peñuela, Isolation of a selected microbial consortium capable of degrading methyl parathion and p-nitrophenol from a contaminated soil site, J. Environ. Sci. Health. B. 46 (2011) 173–180, https://doi.org/10.1080/03601234.2011.539142.
[58] C. Machín-Ramírez, D. Morales, F. Martínez-Morales, A.I. Okoh, M.R. Trejo-Hernández, Benzo[a]pyrene removal by axenic- and co-cultures of some bacterial and fungal strains, Int. Biodeterior. Biodegrad. 64 (2010) 538–544, https://doi.org/10.1016/j.ibiod.2010.05.006.
[59] M. Byss, D. Elhottová, J. Tříska, P. Baldrian, Fungal bioremediation of the creosote-contaminated soil: influence of *Pleurotus ostreatus* and *Irpex lacteus* on polycyclic aromatic hydrocarbons removal and soil microbial community composition in the laboratory-scale study, Chemosphere 73 (2008) 1518–1523, https://doi.org/10.1016/j.chemosphere.2008.07.030.
[60] R. Nazir, J.A. Warmink, H. Boersma, J.D. Van Elsas, Mechanisms that promote bacterial fitness in fungal-affected soil microhabitats, FEMS Microbiol. Ecol. 71 (2010) 169–185, https://doi.org/10.1111/j.1574-6941.2009.00807.x.
[61] L. Ellegaard-Jensen, B.E. Knudsen, A. Johansen, C.N. Albers, J. Aamand, S. Rosendahl, Fungal-bacterial consortia increase diuron degradation in water-unsaturated systems, Sci. Total Environ. 466–467 (2014) 699–705, https://doi.org/10.1016/j.scitotenv.2013.07.095.
[62] A. Dechesne, G. Wang, G. Gülez, D. Or, B.F. Smets, Hydration-controlled bacterial motility and dispersal on surfaces, Proc. Natl. Acad. Sci. U.S.A. 107 (2010) 14369–14372, https://doi.org/10.1073/pnas.1008392107.
[63] G. Wang, D. Or, Aqueous films limit bacterial cell motility and colony expansion on partially saturated rough surfaces, Environ. Microbiol. 12 (2010) 1363–1373, https://doi.org/10.1111/j.1462-2920.2010.02180.x.
[64] L.Y. Wick, R. Remer, B. Würz, J. Reichenbach, S. Braun, F. Schäfer, H. Harms, Effect of fungal hyphae on the access of bacteria to phenanthrene in soil, Environ. Sci. Technol. 41 (2007) 500–505, https://doi.org/10.1021/es061407s.
[65] E.E. Raimondo, J.M. Saez, J.D. Aparicio, M.S. Fuentes, C.S. Benimeli, Bioremediation of lindane-contaminated soils by combining of bioaugmentation and biostimulation: effective scaling-up from microcosms to mesocosms, J. Environ. Manag. 276 (2020) 111309, https://doi.org/10.1016/j.jenvman.2020.111309.
[66] R.J.S. Jacques, B.C. Okeke, F.M. Bento, A.S. Teixeira, M.C.R. Peralba, F.A.O. Camargo, Microbial consortium bioaugmentation of a polycyclic aromatic hydrocarbons contaminated soil, Bioresour. Technol. 99 (2008) 2637–2643, https://doi.org/10.1016/j.biortech.2007.04.047.
[67] P. Chaudhary, R. Sharma, Bioremediation of PAH by *Streptomyces* sp, Bull. Environ. Contam. Toxicol. (2011) 268–271, https://doi.org/10.1007/s00128-011-0211-5.
[68] A.K. Pandey, P. Chaudhary, S.B. Singh, A. Arora, K. Kumar, Deciphering the traits associated with PAH degradation by a novel *Serratia marcesencs* L-11 strain, J. Environ. Sci. Heal. Part A Toxic/Hazardous Subst. Environ. Toxic/Hazardous Subst. Environ. (2012) 37–41, https://doi.org/10.1080/10934529.2012.660108.
[69] E.E. Raimondo, J.M. Saez, J.D. Aparicio, M.S. Fuentes, C.S. Benimeli, Coupling of bioaugmentation and biostimulation to improve lindane removal from different soil types, Chemosphere 238 (2020), https://doi.org/10.1016/j.chemosphere.2019.124512.
[70] E.E. Raimondo, J.D. Aparicio, A.L. Bigliardo, M.S. Fuentes, C.S. Benimeli, Enhanced bioremediation of lindane-contaminated soils through microbial bioaugmentation assisted by biostimulation with sugarcane filter cake, Ecotoxicol. Environ. Saf. 190 (2020) 110143, https://doi.org/10.1016/j.ecoenv.2019.110143.
[71] Y. Lee, S.E. Jeong, M. Hur, S. Ko, C.O. Jeon, Construction and evaluation of a Korean native microbial consortium for the bioremediation of diesel fuel-contaminated soil in Korea, Front. Microbiol. 9 (2018) 1–11, https://doi.org/10.3389/fmicb.2018.02594.
[72] P. Morales, M. Cáceres, F. Scott, L. Díaz-Robles, G. Aroca, A. Vergara-Fernández, Biodegradation of benzo[α]pyrene, toluene, and formaldehyde from the gas phase by a consortium of *Rhodococcus erythropolis* and *Fusarium solani*, Appl. Microbiol. Biotechnol. 101 (2017) 6765–6777, https://doi.org/10.1007/s00253-017-8400-8.
[73] A. Vergara-Fernández, D. Yánez, P. Morales, F. Scott, G. Aroca, L. Diaz-Robles, P. Moreno-Casas, Biofiltration of benzo[A]pyrene, toluene and formaldehyde in air by a consortium of *Rhodococcus erythropolis* and *Fusarium solani*: effect of inlet loads, gas flow and temperature, Chem. Eng. J. 332 (2018) 702–710, https://doi.org/10.1016/j.cej.2017.09.095.
[74] M.S. Fuentes, J.M. Sáez, C.S. Benimeli, M.J. Amoroso, Lindane biodegradation by defined consortia of indigenous *Streptomyces* strains, Water Air Soil Pollut. 222 (2011) 217–231, https://doi.org/10.1007/s11270-011-0818-5.
[75] R.D. Fernandez, N. Bulacio, A. Álvarez, H. Pajot, R. Aragón, Fungal decomposers of leaf litter from an invaded and native mountain forest of NW Argentina, Antonie Leeuwenhoek 110 (2017) 1207–1218, https://doi.org/10.1007/s10482-017-0893-8.
[76] S.B. Costa-Gutierrez, J.D. Aparicio, O.D. Delgado, C.S. Benimeli, M.A. Polti, Use of glycerol for the production of actinobacteria with well-known bioremediation abilities, 3 Biotech 11 (2021), https://doi.org/10.1007/S13205-020-02588-5.

[77] S. Wang, X. Li, W. Liu, P. Li, L. Kong, W. Ren, H. Wu, Y. Tu, Degradation of pyrene by immobilized microorganisms in saline-alkaline soil, J. Environ. Sci. (China) 24 (2012) 1662–1669, https://doi.org/10.1016/S1001-0742(11)60963-7.
[78] M.H. Fulekar, J. Sharma, A. Tendulkar, Bioremediation of heavy metals using biostimulation in laboratory bioreactor, Environ. Monit. Assess. 184 (2012) 7299–7307, https://doi.org/10.1007/s10661-011-2499-3.
[79] G.M. Abdel-Fattah, A.H. Mohamedin, Interactions between a vesicular-arbuscular mycorrhizal fungus (*Glomus intraradices*) and *Streptomyces coelicolor* and their effects on sorghum plants grown in soil amended with chitin of brawn scales, Biol. Fertil. Soils 32 (2000) 401–409, https://doi.org/10.1007/s003740000269.
[80] M. Franco-Correa, A. Quintana, C. Duque, C. Suarez, M.X. Rodríguez, J.M. Barea, Evaluation of actinomycete strains for key traits related with plant growth promotion and mycorrhiza helping activities, Appl. Soil Ecol. 45 (2010) 209–217, https://doi.org/10.1016/j.apsoil.2010.04.007.
[81] F. Kurth, K. Zeitler, L. Feldhahn, T.R. Neu, T. Weber, V. Krištůfek, T. Wubet, S. Herrmann, F. Buscot, M.T. Tarkka, Detection and quantification of a mycorrhization helper bacterium and a mycorrhizal fungus in plant-soil microcosms at different levels of complexity, BMC Microbiol. 13 (2013), https://doi.org/10.1186/1471-2180-13-205.
[82] S.L. Goldstein, J.L. Klassen, *Pseudonocardia* symbionts of fungus-growing ants and the evolution of defensive secondary metabolism, Front. Microbiol. 11 (2020) 1–8, https://doi.org/10.3389/fmicb.2020.621041.
[83] C.R. Currie, J.A. Scott, R.C. Summerbell, D. Malloch, Fungus-growing ants use antibiotic-producing bacteria to control garden parasites, Nature 398 (1999) 701–704.
[84] J. Barke, R.F. Seipke, S. Grüschow, D. Heavens, N. Drou, M.J. Bibb, R.J.M. Goss, D.W. Yu, M.I. Hutchings, A mixed community of actinomycetes produce multiple antibiotics for the fungus farming ant *Acromyrmex octospinosus*, BMC Biol. 8 (2010), https://doi.org/10.1186/1741-7007-8-109.
[85] D. Heine, N.A. Holmes, S.F. Worsley, A.C.A. Santos, T.M. Innocent, K. Scherlach, E.H. Patrick, D.W. Yu, J.C. Murrell, P.C. Vieria, J.J. Boomsma, C. Hertweck, M. I. Hutchings, B. Wilkinson, Chemical warfare between leafcutter ant symbionts and a co-evolved pathogen, Nat. Commun. 9 (2018) 1–11, https://doi.org/10.1038/s41467-018-04520-1.
[86] V. Schroeckh, K. Scherlach, H.-W. Nützmann, E. Shelest, W. Schmidt-Heck, J. Schuemann, K. Martin, C. Hertweck, A.A. Brakhagea, Intimate bacterial – fungal interaction triggers biosynthesis of archetypal polyketides in *Aspergillus nidulans*, Proc. Natl. Acad. Sci. USA 106 (2009) 14558–14563.
[87] H.W. Nützmann, Y. Reyes-Dominguez, K. Scherlach, V. Schroeckh, F. Horn, A. Gacek, J. Schümann, C. Hertweck, J. Strauss, A.A. Brakhage, Bacteria-induced natural product formation in the fungus *Aspergillus nidulans* requires Saga/Ada-mediated histone acetylation, Proc. Natl. Acad. Sci. U.S.A. 108 (2011) 14282–14287, https://doi.org/10.1073/pnas.1103523108.
[88] M.C. Stroe, T. Netzker, K. Scherlach, T. Krüger, C. Hertweck, V. Valiante, A.A. Brakhage, Targeted induction of a silent fungal gene cluster encoding the bacteria-specific germination inhibitor fumigermin, Elife 9 (2020) 1–20, https://doi.org/10.7554/eLife.52541.
[89] M. Moussa, W. Ebrahim, M. Bonus, H. Gohlke, A. Mándi, T. Kurtán, R. Hartmann, R. Kalscheuer, W. Lin, Z. Liu, P. Proksch, Co-culture of the fungus *Fusarium tricinctum* with *Streptomyces lividans* induces production of cryptic naphthoquinone dimers, RSC Adv. 9 (2019) 1491–1500, https://doi.org/10.1039/C8RA09067J.
[90] M. Yu, Y. Li, S.P. Banakar, L. Liu, C. Shao, Z. Li, C. Wang, New metabolites from the co-culture of marine-derived actinomycete *Streptomyces rochei* MB037 and fungus *Rhinocladiella similis* 35, Front. Microbiol. 10 (2019) 1–11, https://doi.org/10.3389/fmicb.2019.00915.
[91] C. Wu, B. Zacchetti, A.F.J. Ram, G.P. Van Wezel, D. Claessen, Y.H. Choi, Expanding the chemical space for natural products by *Aspergillus-Streptomyces* co-cultivation and biotransformation, Sci. Rep. 5 (2015), https://doi.org/10.1038/srep10868.
[92] L. Yu, W. Ding, Z. Ma, Induced production of cytochalasans in co-culture of marine fungus *Aspergillus flavipes* and actinomycete *Streptomyces* sp, Nat. Prod. Res. 30 (2016) 1718–1723, https://doi.org/10.1080/14786419.2015.1136910.
[93] P.A. Martínez-Buitrago, F.A. Ramos, L. Castellanos, Binary co-culture selection from marine-derived microorganisms for differential production of specialized metabolites, Quim. Nova 42 (2019) 713–719, https://doi.org/10.21577/0100-4042.20170388.
[94] A. Ścigaczewska, T. Boruta, M. Bizukojć, Quantitative morphological analysis of filamentous microorganisms in cocultures and monocultures: *Aspergillus terreus* and *Streptomyces rimosus* warfare in bioreactors, Biomolecules 11 (2021) 1–22, https://doi.org/10.3390/biom11111740.
[95] K.W. Siemieniewicz, H. Schrempf, Concerted responses between the chitin-binding protein secreting *Streptomyces olivaceoviridis* and *Aspergillus proliferans*, Microbiology 153 (2007) 593–600, https://doi.org/10.1099/mic.0.2006/001073-0.
[96] C.C. König, K. Scherlach, V. Schroeckh, F. Horn, S. Nietzsche, A.A. Brakhage, C. Hertweck, Bacterium induces cryptic meroterpenoid pathway in the pathogenic fungus *Aspergillus fumigatus*, Chembiochem 14 (2013) 938–942, https://doi.org/10.1002/cbic.201300070.
[97] K.F. Chater, S. Biró, K.J. Lee, T. Palmer, H. Schrempf, The complex extracellular biology of *Streptomyces*, FEMS Microbiol. Rev. 34 (2010) 171–198, https://doi.org/10.1111/j.1574-6976.2009.00206.x.
[98] Y.S. Yang, J.T. Zhou, H. Lu, Y.L. Yuan, L.H. Zhao, Isolation and characterization of *Streptomyces* spp. strains F-6 and F-7 capable of decomposing alkali lignin, Environ. Technol. 33 (2012) 2603–2609, https://doi.org/10.1080/09593330.2012.672473.