doi:10.2533/chimia.2022.939 Chimia 76 (2022) 939–944

Microbes to the Rescue – Exploring the Chemistry of Microbial Communication and Using it to Protect Plant Health

Laure Weisskopf*

Abstract: Plants are densely colonized by diverse microbial communities. These microbes, which provide important benefit to their host supporting its growth and health, interact with each other and with their host plant by exchanging chemical signals, including volatile organic compounds (VOCs). This review presents some of our current research lines in the field of microbial VOCs, including their bioactivities on both plants and plant pathogens, and the abiotic and biotic factors influencing their emission. Understanding how VOCs emission is regulated in plant-associated microbes is one of the major challenges for both fundamental and translational aspects of this research field.

Keywords: Bacteria · Fungi · Phytopathogens · Volatiles

Laure Weisskopf obtained her PhD in 2005 at the University of Neuchâtel in the field of plant–microbe interactions. After a post-doctoral stay in Kenya, she stayed until 2012 at the University of Zurich, where she started her independent research focusing on bacterial volatiles and their impact on plants. She then spent a couple of years in applied research institutions (Agroscope and HES-SO Changins) until 2017 where she was appointed Professor for plant-microbe interactions at the University of Fribourg. Her group's research focuses on understanding how plant-associated microbes communicate and on translating these findings into more sustainable crop protection practices.

1. Microbes are Prolific Producers of Specialized Metabolites

Specialized metabolites, formerly also referred to as 'secondary metabolites', are compounds that are not directly involved in the survival of the producing organisms in ideal growth conditions but that are very often crucial to their fitness in their natural environments, since they play a role in mediating a wide range of ecological interactions with other organisms, as well as in conferring tolerance to a large spectrum of stressing factors. When thinking of the most prolific producers of such specialized metabolites, plants are usually the first organisms that come to mind. Plants as sessile organisms needed to develop sophisticated ways to chemically attract beneficial interactors (*e.g.* pollinators) or repel threatening ones (*e.g.* herbivores).[1]

However, next to plants, microbes – and especially bacteria – also deserve attention when it comes to the discovery of new specialized metabolites, for many reasons including: i) bacteria have been diversifying and adapting to different environments since life arose on the planet, leading to an extreme phylogenetic and metabolic diversity, ii) their fast growth rate and exchange of genetic elements enabled rapid evolution and adaptation to new niches and substrates, with concomitant changes in metabolite production, iii) bacteria can grow as autotrophs or heterotrophs, in oxic or anoxic conditions, as free-living organisms in water, soil and air, or in association with different hosts, thus exploiting a diversity of niches and nutrients, which themselves lead to the production of different metabolomes, iv) they engage in multifaceted interactions with other microbes, plants and animals and use specialized metabolites to mediate these interactions, and last but not least v) many bacteria are yet to be discovered, cultured and explored for their specialized metabolism, whereas we have a much better overview of plants and of the other macroscopic organisms colonizing our planet.

Most efforts in characterizing specialized metabolites in the bacterial kingdom have focused so far on filamentous bacteria called Actinomycetes (*e.g. Streptomyces* species) to whom we owe a majority of our past and current antibiotics as well as many other bioactive compounds.[2] These fascinating fungi-like prokaryotes produce a very typical specialized metabolite, the volatile terpene geosmin, which is responsible for the soil-like odor we smell when we walk through a forest. This compound was recently shown to not only attract mosquitoes and flies, but also soil arthropods, which contributed to the dispersal of the geosmin-emitting bacteria.[3]

Beyond geosmin, Actinomycetes and other bacteria produce a plethora of volatile organic compounds (VOCs) of diverse chemical structures, biochemical origins and biological functions.[4] Some of them originate from primary metabolism (*e.g.* fermentation products) and are hence shared between many different bacteria, while others are produced from more specific pathways that could be considered as specialized metabolites and are found only in few taxonomic groups (please see ref. [4] for a more comprehensive overview of these different VOC categories). Despite their diversity, VOCs share several common features, such as a low boiling point, a low molecular weight and the presence of a lipophilic moiety. VOCs as communication messengers have long been thought to be restricted to gaseous environments, yet they are also able to diffuse in aqueous solutions, and are even thought to do so faster due to lack of a hydration sphere.[4] As such, they can be considered early alert signals in the chemical communication establishing when two interacting organisms come closer to each other. This can occur in a variety of environments, yet our research group has a longstanding interest in bacteria interacting with plants, and this is what this review focuses on.

*Correspondence: Prof. Dr. L. Weisskopf, E-mail: laure.weisskopf@unifr.ch
Department of Biology, University of Fribourg, CH-1700 Fribourg

2. Plant-associated Bacteria Emit Volatiles that Modulate Plant Growth and Health

Plants are colonized by a wide diversity of microbes from roots to shoots,[5] as shown in the leaf imprint depicted in Fig. 1.

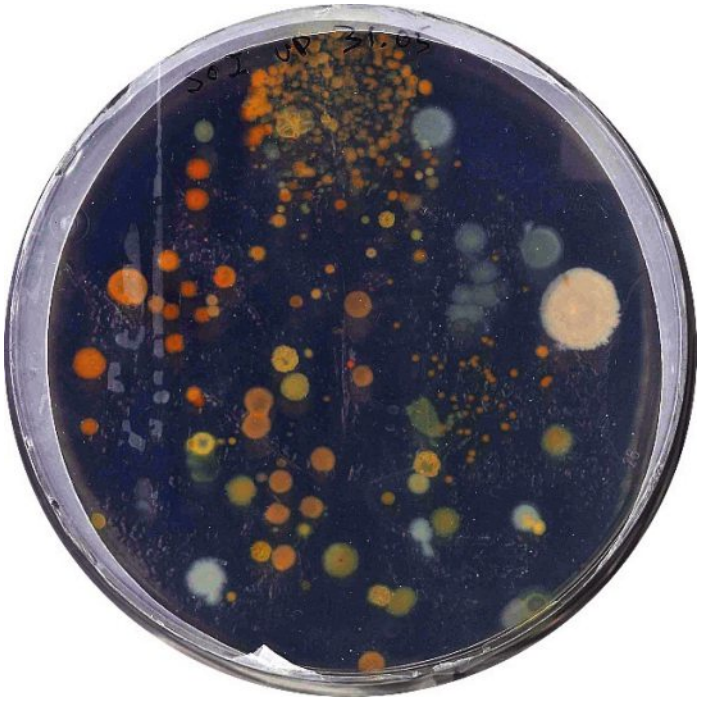

Fig. 1. Imprint of a young grapevine leaf (cv. Solaris) on a minimal cultivation medium containing glucose as a carbon source, illustrating dense leaf surface colonization by different bacteria.

This agar medium plate was imprinted with a grapevine leaf, which led to the formation of multiple bacterial colonies of different shapes and sizes, illustrating the diversity of cultivable leaf-associated bacteria, which represent just a small part of the entire leaf microbiota. The fact that most colonies are colored is a typical feature of leaf-associated bacteria and highlight their need for UV protection in this highly exposed environment.

Beyond leaf-associated bacteria, plant roots are also densely populated by bacterial communities originating to a large extent from the soil. Most of the plant microbiota members are heterotrophs, *i.e.* they rely on organic carbon provided by a primary producer such as the plant. In exchange, bacteria can help the plant to acquire mineral nutrients such as nitrogen or phosphorous, or promote plant growth in different ways, *i.e.* by producing phytohormones involved in growth and development.

Bacteria displaying one or more of these plant-beneficial traits are called plant growth promoting rhizobacteria (PGPR). In 2003, a ground-breaking paper reported highly significant growth promotion in plants solely exposed to VOCs emitted by a selection of PGPR strains.[6] This prompted the development of a new research field, devoted to understanding the nature and function of VOC emission by plant-associated bacteria. It was soon discovered that the ability to strongly modulate plant growth was not restricted to the few initially described PGPR strains, but a rather general feature of plant-associated bacteria, which strongly depended on their growth phase[7] and on the cultivation media used to grow them.[8]

Acetoin and 2,3-butanediol, which are the end products of a specific fermentation pathway some bacteria use to avoid excessive acidification of their environment, were the first compounds reported as responsible for the observed growth promotion,[6] later followed by other small volatiles such as indole[9] or dimethyl disulfide.[10] Early reports also described that in addition to promoting growth, microbial VOCs also promoted the health of plants. Such plant health protection could originate from mainly two different mechanisms: i) the stimulation of the plant immune system, and ii) the inhibition of plant pathogens.

2.1 *Microbial Volatiles Inducing Plant Resistance*

Soon after the discovery of 2,3-butanediol's impact on growth, the same molecule produced by different bacteria was implicated in triggering disease resistance in the model plant *Arabidopsis thaliana*,[11,12] and later also on other plants of agronomical relevance such as pepper and cucumber.[13,14] Other VOCs of similar structure such as 3-pentanol or 3-butanone were also able to elicit disease resistance in greenhouse or even open-field grown plants,[15,16] suggesting potential use of these molecules as bioprotectants (see below, section 4), while the higher concentrations necessary to trigger resistance by exposing plants to the long-chain alkane tridecane preclude the use of this compound under field conditions.[17] In addition to stimulating the immune system of their host, plant-associated bacteria have another, potentially more powerful way to promote its health, namely by inhibiting the growth and development of disease-causing agents.

2.2 *Microbial Volatiles Inhibiting Plant Pathogens*

Compared to the relatively few studies reporting the induction of plant resistance described above, a plethora of reports describes the antimicrobial effects of microbial VOCs. This should not come as a surprise, given the different ecological interactions occurring between microbes and plants vs. between microbes themselves: in plant–microbe interactions, both partners clearly benefit from each other as highlighted above (exchanging organic carbon for mineral nutrients, phytohormones or other). However, heterotrophic microbes (the majority of plant-associated bacteria and all fungi) compete with each other for the very same organic carbon fixed by the plants, as well as for other resources such as iron, an abundant but poorly available nutrient for both plant- and soil-inhabiting microbes.

Microbial volatiles with reported inhibitory activities on disease-causing agents of bacterial, fungal or oomycete origin are diverse both chemically and in terms of the organisms which produce them (reviewed in refs [18,19]).

Beyond the respiratory toxin HCN, which was one of the first volatiles to be implicated in such plant health protection mediated by plant-associated *Pseudomonas*,[20] sulfur (S)-containing volatiles have been repeatedly reported to inhibit different developmental stages of fungal and oomycete pathogens, such as spore production, motility or germination, as well as mycelial growth.[21–24] Some of these S-VOCs have even been suggested as next-generation biofumigants to replace the infamous and meanwhile prohibited methyl bromide. While some of these compounds show a too high toxicity on non-target organisms to be useful for field application,[25] others (such as dimethyl disulfide) are already commercialized for soil fumigation[26,27] despite reported toxic effects.[28]

Clearly, the abundant body of literature reporting antimicrobial effects of microbial VOCs on plant pathogens highlights them as a rich source of new biopesticides, but whether their application (as pure compounds) to replace currently used synthetic pesticides is a promising approach remains debatable, and is discussed further in section 4.

One important aspect of microbial VOCs emission, which is still very poorly understood, is whether these compounds are constitutively produced or whether they are induced by specific factors. As mentioned above and detailed in ref. [4], this will depend on whether they are simply 'waste products' of the primary metabolism with additional biological effects on target organisms

(such as plant pathogens) or whether their emission responds to specific needs of the producing strains facing particular situations. In this latter case, the compounds would not be detected in classical sampling experiments, where the headspace of a pure culture growing alone in 'ideal' conditions in the laboratory is collected without exposing the strains to the abiotic and biotic factors that would lead to the requirement for and hence induction of these compounds' emission.

In terms of abiotic factors, the observation that the emission of VOCs by the same strain varies strongly depending on the cultivation media[8,29,30] is a clear indicator that the available nutrients are a major determinant in the composition of the VOCs blends. Beyond nutrients, other parameters such as pH or oxygen tension are likely to play an important role too, as major drivers of bacterial physiology and metabolism. In addition to these abiotic factors, one would expect microbial VOCs involved in biotic interactions to be triggered by the presence of the interacting partner. This question, which is still poorly investigated, is at the core of our current research interests and is addressed in the following section.

3. Dialogue rather than Monologue: Elucidating the Biotic Factors Influencing Microbial Volatile Emission

In 2017, researchers demonstrated for the first time that exposing a bacterium to the VOCs emitted by an interacting partner (fungus) led not only to massive reprogramming of the bacterial physiology (including changes in motility, nitrogen acquisition or energy metabolism) but also to the emission of the volatile terpene sodorifen.[31] This brought the proof of concept that bacteria are able to perceive volatile cues from neighboring microbes and to react accordingly, including *via* the emission of new VOCs.

3.1 *Microbes Detect each other's Volatiles*

This ability to modulate volatile emission depending on neighboring organisms is of particular relevance considering that in their natural environments, microbes are not found in pure cultures such as those studied in most laboratories, but in complex communities. Among bacterial communities, several studies have shown that the VOCs emitted by multiple species are more than the sum of the VOCs emitted by each species individually.[32–35] Such interactions occur not only within bacterial communities, but as mentioned above for the example of sodorifen, interkingdom interactions between fungi and bacteria also occur *via* VOCs. One way to visualize such interactions is to co-incubate both organisms and to monitor changes in the physiology of one or the other partner. Using such experimental setups, Schmidt and co-workers demonstrated increased motility of several bacteria exposed to the VOCs emitted by different fungi and oomycetes,[36] indicating that VOCs are used as cues to recognize the presence of an interacting organism and to move towards (or away from) it.

As mentioned above, iron is an important player in many microbial interactions because of its scarce availability. As a consequence, many microbes produce soluble siderophores (*i.e.* small molecules with high affinity for iron) to increase their access to this important micronutrient. As illustrated in Fig. 2, exposing a *Trichoderma* fungus to the VOCs emitted by a *Pseudomonas* bacterium led to increased siderophore secretion by the fungus. In this case, the fungus was not inhibited in its growth by the emitted bacterial VOCs, but still reacted to the presence of a putative iron competitor by higher investment in siderophore production. When exposed to different interacting partners (*e.g.* another fungus instead of the bacterium), the same behavior was observed, but this time linked to a decreased growth phenotype.

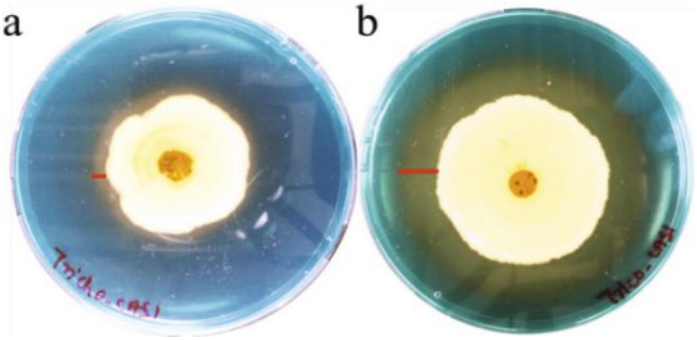

Fig. 2. Siderophore production increases in a *Trichoderma* strain (white colony) exposed to volatiles from a *Pseudomonas* strain (not visible on this picture). Representative pictures from a plate overlay experiment where *Trichoderma* was grown on CAS medium (allowing visualization of siderophores as orange halo around the fungal colony) and overlaid with another plate containing either *Trichoderma* (negative ctrl) (a) or *Pseudomonas* (b). Only volatiles can be exchanged between the two partners in this plate overlay set-up. The red line indicates the diffusion zone of the siderophores.

3.2 *Substantial Shifts in Volatile Emission Occur in Presence of an Interacting Partner*

In the above illustration and in many similar interaction studies where altered behaviors or shifts in emitted VOCs were observed (recently reviewed in ref. [37]), we observe measurable effects of the interaction but cannot disentangle which organism triggered which change in the other, *via* which signaling compound. In an attempt to solve this problem limiting our understanding of the mechanisms underlying the observed effects of microbial interactions, we have designed a volatile sampling system allowing sequential exposure of one interacting partner to the VOCs emitted by the other.

By connecting two custom-made Teflon microcosms, which we normally use to collect the VOCs of one pure microbial culture at a time with a closed-loop stripping apparatus described in refs [21,38], we can build an open VOCs sampling system allowing unidirectional flow of air from one partner to the other. This allows exposure of one organism to the VOCs emitted by the other without reciprocal influence of the recipient on the emitter, which can later be assessed in a separate experiment by inverting the order of the microcosms connected in series, whereby the former emitter becomes the recipient and vice-versa. Using the appropriate controls (organisms grown alone and/or exposed to the empty medium used to grown the interacting partner) allows to compare the VOCs emitted constitutively and those induced/repressed upon sensing of the interacting organism's VOCs.

In such a system, if no interaction takes place between the two organisms, the volatiles collected should correspond to the addition of those emitted by both organisms grown alone. Any shifts from this control situation, however, could potentially indicate induced or repressed synthesis of VOCs by the exposed organism upon sensing of the emitter's VOCs. In addition to such biological induction or repression, however, new compounds could also be generated by chemical reaction not involving any specific induction, as reported recently for schleiferon.[35]

As an example of outcome of such interaction experiments, Fig. 3 shows an overlay of different chromatograms corresponding to the VOCs emitted by a plant growth promoting fungus (*Trichoderma* strain, used here as VOCs recipient) grown alone (pink), by a plant pathogenic fungus (*Fusarium* strain, used here as VOCs emitter) grown alone (red), and by *Trichoderma* exposed to the VOCs of *Fusarium* (green), whereas the blue chromatogram shows VOCs detected when sampling the empty growth medium.

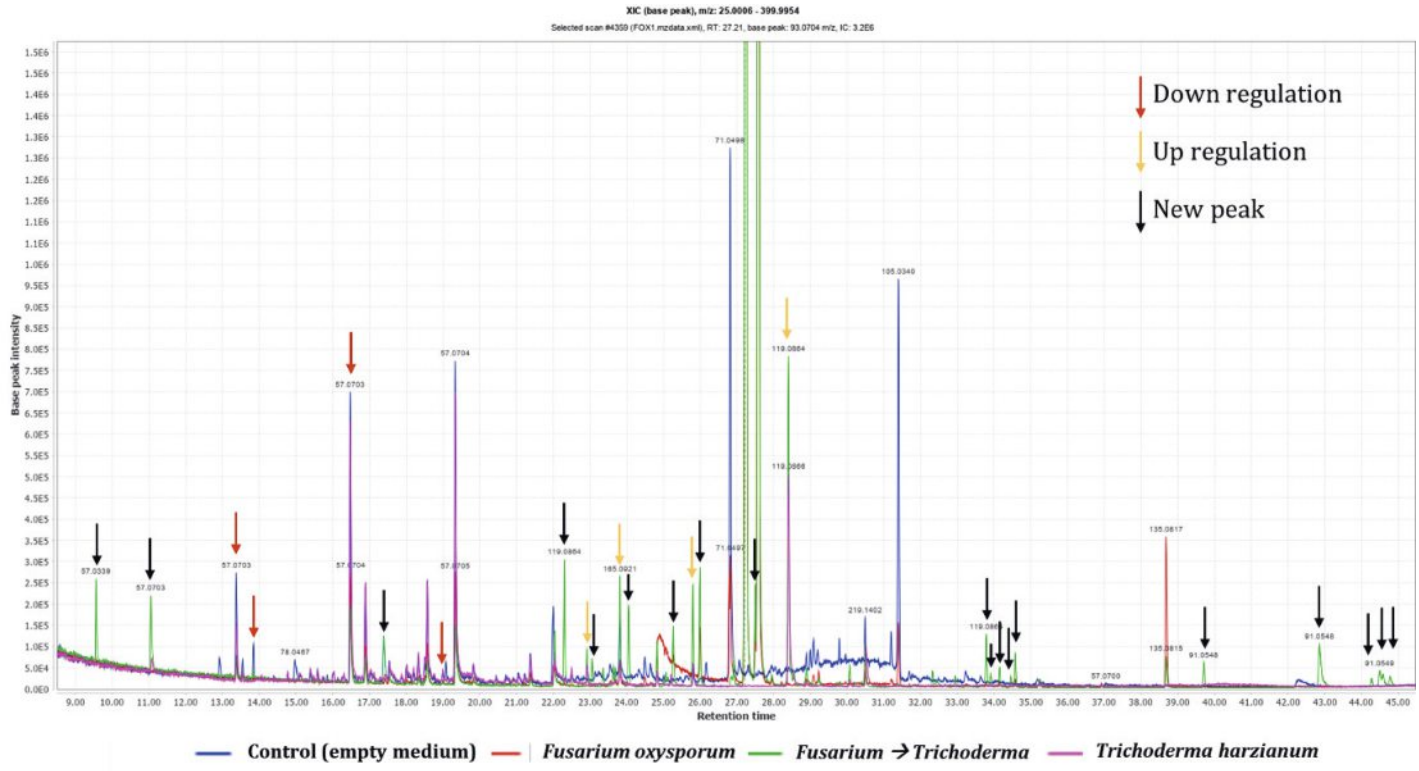

Fig. 3. Shifts in the VOCs profiles of *Trichoderma* exposed to *Fusarium* (green) compared with *Trichoderma* grown alone (pink), *Fusarium* grown alone (red) and the empty medium control (blue). Representative chromatograms for each treatment were overlaid to visualize peaks with decreased abundance (red arrows), increased abundance (yellow arrows), or newly detected peaks (black arrows).

As expected, substantial shifts can be observed when comparing the chromatogram of the exposed (green) to that of the non-exposed (pink) *Trichoderma*. In addition to quantitative changes which should be interpreted with care in the absence of an internal standard, numerous peaks were detected only in the volatile profile of exposed *Trichoderma*, indicating global modulation of volatile emission rather than a response restricted to few regulated enzymes, leading only to few induced VOCs. The substantial shift in emitted VOCs between an organism grown alone and one exposed to chemical cues of an interacting partner has practical implications for the discovery of new, potentially bioactive compounds and highlights the need to integrate such biological interactions into drug discovery projects.

Indeed, few reports already pointed out that direct (*i.e.* not volatile-mediated) biological interactions led to the production of more compounds of interest (*e.g.* antibiotics) in the interacting strains.[32,39,40] Such induction might therefore also be occurring when only volatiles are exchanged between the two partners, as suggested by our analysis of the interaction between *Trichoderma* and *Fusarium* or by the induction of siderophore production in *Trichoderma* upon sensing of VOCs emitted by *Pseudomonas* bacteria.

Although this biological context-dependent VOCs emission certainly adds an extra layer of complexity to the challenging task of disentangling the chemical communication taking place within plant-associated microbiota, this also represents a great opportunity not only to discover new compounds, but also to harness their bioactivity for applied purposes such as the protection of plant health, as discussed below.

4. Future Challenges

Since the discovery of the plant growth promoting activity of bacterial volatiles in 2003,[6] this field of research has substantially expanded, unravelling a plethora of microbial strains (bacteria, fungi, but also protists) emitting complex blends of VOCs with diverse effects on as diverse target organisms, mainly plants and plant pathogens, while reports on animals are less numerous. Given this focus on plants and the concomitant gradual discovery of the key roles the plant microbiota plays in the health of its host,[5,41] attempts to apply VOCs-emitting strains or VOCs as pure compounds/mixtures to protect plants against diseases have also started early. However, both the fundamental understanding of the causes and consequences of VOCs emission for plant–microbe and microbe–microbe communication, and its translational potential face a certain number of challenges, which are briefly outlined in the following sections.

4.1 *Major Knowledge Gaps*

Despite two decades of research, we still understand very little of the genetic determinants of VOCs emission, nor of the inducing factors (see above) triggering their emission. After the first phase of descriptive work this field of research has witnessed, it is time to move on to, on one side, more mechanistic studies using molecular tools (*e.g.* mutant generation and screens) in genetically tractable model organisms, and on the other side, experimental setups coming closer to the natural situation of complex communities living on plant surface rather than on artificial media. Along these lines, few reports have already shown that VOCs of relevant biological activities are not only emitted by microbes grown on nutrient-rich media, but also by those living in the soil[34] or on plant leaves.[42] In addition to growth conditions approaching those of the microbes' natural environment, the biotic factors highlighted as leading to substantial shifts in VOCs emission should be integrated as well, going much beyond the 1:1 interaction described above, towards more and more complex communities. Deciphering who emits which compound and with which consequences on which target organism is unlikely to be achieved in such complex systems in the near future, but overall shifts in VOCs profiles upon introduction of a new community member, of a change in the health status of the host plants or its root exudation profile, *etc.* could be measured as a next step to take to come closer to the reality of microbial communication in the

plant microbiota. Coupling such VOCs profiling with other global analyses such as metatranscriptomics or metaproteomics could help identifying the VOC emitters, the enzymes involved and the molecular targets of the emitted VOCs, which however in view of the technical challenges inherent to each of these techniques might only become possible in a couple of decades.

On the side of the recipients (target organisms), we still know very little about the modes of action leading to the phenotypic changes we observe upon exposure to microbial VOCs. Some of these molecules are likely to interfere with membrane integrity or to cause oxidative stress,[4] but except for few pioneer studies,[43,44] we are still lacking mechanistic insights into how VOCs are perceived by target organisms, whether they enter cells or are perceived externally by receptors, and which signaling pathways are involved in mediating the phenotypic changes we ultimately observe in our biological assays. When characterizing the effect of various S-VOCs on the oomycete *Phytophthora infestans* causing late blight in potato, we observed multiple dysregulated functions, going from perturbed S-cycle to oxidative stress or impaired ribosomal functions.[22] Such understanding of the modes of action of VOCs is not only relevant for our understanding of the underlying mechanisms but also necessary to envisage the range of non-target effects to be expected and hence the likelihood of a given compound being suitable for application.

4.2 *Translational Potential for Crop Health*

Before we can translate to the field the promising effects obtained in laboratory, *e.g*. on the growth inhibition of various plant pathogens or even on the *in planta* protection against diseases observed in pot experiments, another set of challenges needs to be addressed.

The first and likely most important one relates to the potential toxicity of the active VOCs. One recent example from our research highlighted that absence of phytotoxicity of a S-VOC with highly promising activity against the late blight causing agent did not preclude toxic effects on other organisms, such as bacteria in this particular case.[25] Moreover, replacing synthetic pesticides with 'natural' ones may warrant better biodegradability and hence lesser environmental accumulation, but other problems such as non-target effects or the development of resistance in the targeted organism, remain the same.

To overcome these two problems, a promising approach would lie in using the VOC-emitting strains rather than the pure chemical compounds, provided the introduced microbes manage to establish in sufficient population densities and – which might be even more challenging – they emit the desired VOCs *in situ*.

In this regard, our attempts to gain a fundamental understanding of the factors underlying induction of specific VOC emission might translate into very useful knowledge for practical application, should such triggering factors be able to stimulate already established microbiota to emit plant health-protecting VOCs where and when needed by the plant.

5. Conclusion

Despite substantial progress in this field of research since its birth two decades ago, much remains to be done to unravel the complex but fascinating chemical dialogue occurring between different members of the plant microbiota, as well as between the plant and its associated microbial communities. In view of the pressing need for alternative crop health protecting measures, it is our hope that at least some of the promising plant protecting effects observed in controlled conditions will make their way to the open field and be integrated into future and more sustainable food production systems.

Acknowledgements

I am grateful to the members of my research group for their excellent work and wish to specifically thank Dr. Alsayed Alfiky and Dr. Sébastien Bruisson for providing the material shown in Figs. 2 and 3. Their work has been partially supported by the Swiss National Science Foundation through grant nr. 179310.

Received: August 12, 2022

[1] D. Marone, A. M. Mastrangelo, G. M. Borrelli, A. Mores, G. Laidò, M. A. Russo, D. B. M. Ficco, *Plant Physiol. Biochem*. **2022**, *172*, 48, https://doi.org/10.1016/j.plaphy.2021.12.037.
[2] E. Ait Barka, P. Vatsa, L. Sanchez, N. Vaillant-Gaveau, C. Jacquard, H.-P. Klenk, C. Clément, Y. Ouhdouch, P. Van Wezel, *Microbiol. Mol. Biol. Rev*. **2016**, *80*, 1, https://doi.org/10.1128/MMBR.00019-15.Address.
[3] P. G. Becher, V. Verschut, M. J. Bibb, M. J. Bush, B. P. Molnár, E. Barane, M. M. Al-Bassam, G. Chandra, L. Song, G. L. Challis, M. J. Buttner, K. Flärdh, *Nat. Microbiol*. **2020**, 1, https://doi.org/10.1038/s41564-020-0697-x.
[4] L. Weisskopf, S. Schulz, P. Garbeva, *Nat. Rev. Microbiol*. **2021**, *19*, 391, https://doi.org/10.1038/s41579-020-00508-1.
[5] D. B. Müller, C. Vogel, Y. Bai, J. A. Vorholt, *Annu. Rev. Genet*. **2016**, *50*, 211, https://doi.org/10.1146/annurev-genet-120215-034952.
[6] C.-M. Ryu, M. a Farag, C.-H. Hu, M. S. Reddy, H.-X. Wei, P. W. Paré, J. W. Kloepper, *Proc. Natl. Acad. Sci. U. S. A*. **2003**, *100*, 4927, https://doi.org/10.1073/pnas.0730845100.
[7] M. Kai, E. Crespo, S. M. Cristescu, F. J. M. Harren, W. Francke, B. Piechulla, *Appl. Microbiol. Biotechnol*. **2010**, *88*, 965, https://doi.org/10.1007/s00253-010-2810-1.
[8] D. Blom, C. Fabbri, E. C. Connor, F. P. Schiestl, D. R. Klauser, T. Boller, L. Eberl, L. Weisskopf, *Environ. Microbiol*. **2011**, *13*, 3047, https://doi.org/10.1111/j.1462-2920.2011.02582.x.
[9] A. Bailly, U. Groenhagen, S. Schulz, M. Geisler, L. Eberl, L. Weisskopf, *Plant J*. **2014**, 80, 758, https://doi.org/10.1111/tpj.12666.
[10] D. G. Meldau, S. Meldau, L. H. Hoang, S. Underberg, H. Wünsche, I. T. Baldwin, H. Wunsche, I. T. Baldwin, *Plant Cell* **2013**, *25*, 2731, https://doi.org/10.1105/tpc.113.114744.
[11] C.-M. Ryu, M. A. Farag, C.-H. Hu, M. S. Reddy, J. W. Kloepper, P. W. Paré, *Plant Physiol*. **2004**, *134*, 1017, https://doi.org/10.1104/pp.103.026583.
[12] S. H. Han, S. J. Lee, J. H. Moon, K. H. Park, K. Y. Yang, B. H. Cho, K. Y. Kim, Y. W. Kim, M. C. Lee, A. J. Anderson, Y. C. Kim, *Mol. Plant. Microbe. Interact*. **2006**, *19*, 924, https://doi.org/10.1094/MPMI-19-0924.
[13] H. G. Kong, T. S. Shin, T. H. Kim, C.-M. Ryu, *Front. Plant Sci*. **2018**, *9*, 90, https://doi.org/10.3389/fpls.2018.00090.
[14] G. C. Song, M. Riu, C.-M. Ryu, *Plant Methods* **2019**, *15*, 9, https://doi.org/10.1186/s13007-019-0395-y.
[15] H. K. Choi, G. C. Song, H. S. Yi, C. M. Ryu, *J. Chem. Ecol*. **2014**, *40*, 882, https://doi.org/10.1007/s10886-014-0488-z.
[16] G. C. Song, C. M. Ryu, *Int. J. Mol. Sci*. **2013**, *14*, 9803, https://doi.org/10.3390/ijms14059803.
[17] B. Lee, M. A. Farag, H. B. Park, J. W. Kloepper, S. H. Lee, C. M. Ryu, *PLoS One* **2012**, *7*, e48744, https://doi.org/10.1371/journal.pone.0048744.
[18] L. Weisskopf, 'The potential of bacterial volatiles for crop protection against phytophathogenic fungi'in 'Microbial pathogens and strategies for combating them science, technology and education', Ed. A. Méndez-Vilas, Formatex Research Center, Badajoz, **2013**, p. 1352.
[19] B. Piechulla, M.-C. Lemfack, M. Kai, *Plant. Cell Environ*. **2017**, *40*, 2042, https://doi.org/10.1111/pce.13011.
[20] C. Voisard, C. Keel, D. Haas, G. Defago, *EMBO J.* **1989**, *8*, 351, https://doi.org/10.1002/j.1460-2075.1989.tb03384.x.
[21] M. De Vrieze, P. Pandey, T. D. Bucheli, A. R. Varadarajan, C. H. Ahrens, L. Weisskopf, A. Bailly, *Front. Microbiol.* **2015**, *6*, 1295, https://doi.org/10.3389/fmicb.2015.01295.
[22] D. Chinchilla, S. Bruisson, S. Meyer, D. Zühlke, C. Hirschfeld, C. Joller, F. L'Haridon, L. Mène-Saffrané, K. Riedel, L. Weisskopf, *Sci. Rep*. **2019**, https://doi.org/10.1038/s41598-019-55218-3.
[23] N. Dandurishvili, N. Toklikishvili, M. Ovadis, P. Eliashvili, N. Giorgobiani, R. Keshelava, M. Tediashvili, A. Vainstein, I. Khmel, E. Szegedi, L. Chernin, *J. Appl. Microbiol*. **2011**, *110*, 341, https://doi.org/10.1111/j.1365-2672.2010.04891.x.
[24] C. Sá, D. Matos, A. Pires, P. Cardoso, E. Figueira, *Sci. Total Environ*. **2021**, *800*, 149478, https://doi.org/10.1016/j.scitotenv.2021.149478.
[25] C. Joller, M. De Vrieze, A. Moradi, C. Fournier, D. Chinchilla, F. L. Haridon, S. Bruisson, L. Weisskopf, *Pathogens* **2020**, *9*, 496, https://doi.org/10.3390/pathogens9060496.
[26] M. A. Gómez-Tenorio, J. C. Tello, M. J. Zanón, M. de Cara, *Crop Prot*. **2018**, *112*, 133, https://doi.org/10.1016/j.cropro.2018.05.023.
[27] J. A. Cabrera, D. Wang, J. S. Gerik, J. Gan, *Pest Manag. Sci*. **2014**, *70*, 1151, https://doi.org/10.1002/ps.3666.

[28] P. R. Mulay, P. Cavicchia, S. M. Watkins, A. Tovar-Aguilar, M. Wiese, G. M. Calvert, *J. Agromedicine* **2016**, *21*, 373, https://doi.org/10.1080/1059924X.2016.1211574.
[29] V. Lazazzara, M. Perazzolli, I. Pertot, F. Biasioli, G. Puopolo, L. Cappellin, *Microbiol. Res*. **2017**, *201*, 52, https://doi.org/10.1016/j.micres.2017.04.015.
[30] W. Raza, J. Yuan, N. Ling, Q. Huang, Q. Shen, *Biol. Control* **2015**, *80*, 89, https://doi.org/10.1016/j.biocontrol.2014.09.004.
[31] R. Schmidt, V. De Jager, D. Zühlke, C. Wolff, J. Bernhardt, K. Cankar, J. Beekwilder, W. Van Ijcken, F. Sleutels, W. De Boer, K. Riedel, P. Garbeva, *Sci. Rep*. **2017**, *7*, 1, https://doi.org/10.1038/s41598-017-00893-3.
[32] O. Tyc, V. C. L. de Jager, M. van den Berg, S. Gerards, T. K. S. Janssens, N. Zaagman, M. Kai, A. Svatos, H. Zweers, C. Hordijk, H. Besselink, W. de Boer, P. Garbeva, *Microb. Biotechnol*. **2017**, *10*, 910, https://doi.org/10.1111/1751-7915.12735.
[33] O. Tyc, H. Zweers, W. de Boer, P. Garbeva, *Front. Microbiol*. **2015**, *6*, 1412, https://doi.org/10.3389/fmicb.2015.01412.
[34] K. Schulz-Bohm, H. Zweers, W. de Boer, P. Garbeva, *Front. Microbiol*. **2015**, *6*, 1212, https://doi.org/10.3389/fmicb.2015.01212.
[35] M. Kai, U. Effmert, M. C. Lemfack, B. Piechulla, *Sci. Rep*. **2018**, *8*, 16852, https://doi.org/10.1038/s41598-018-35341-3.
[36] R. Schmidt, D. W. Etalo, V. de Jager, S. Gerards, H. Zweers, W. de Boer, P. Garbeva, *Front. Microbiol*. **2016**, *6*, 1, https://doi.org/10.3389/fmicb.2015.01495.
[37] S. Bruisson, G. Berg, P. Garbeva, L. Weisskopf, in 'Bacterial Volatile Compounds as Mediators of Airborne Interactions', Springer ed., Eds. C.-M. Ryu, L. Weisskopf, B. Piechulla, **2020**, pp. 215.
[38] U. Groenhagen, R. Baumgartner, A. Bailly, A. Gardiner, L. Eberl, S. Schulz, L. Weisskopf, *J. Chem. Ecol*. **2013**, *39*, 892, https://doi.org/10.1007/s10886-013-0315-y.
[39] J. Barke, R. F. Seipke, S. Grüschow, D. Heavens, N. Drou, M. J. Bibb, R. J. Goss, D. W. Yu, M. I. Hutchings, *BMC Biol*. **2010**, 8, https://doi.org/10.1063/1.2810343.
[40] C. Zhang, P. D. Straight, *Curr. Opin. Microbiol*. **2019**, *51*, 64, https://doi.org/10.1016/j.mib.2019.06.006.
[41] P. Trivedi, J. E. Leach, S. G. Tringe, T. Sa, B. K. Singh, *Nat. Rev. Microbiol*. **2020**, *18*, 607, https://doi.org/10.1038/s41579-020-0412-1.
[42] A. Gfeller, P. Fuchsmann, M. De Vrieze, K. Gindro, L. Weisskopf, *Microorganisms* **2022**, *10*, 1510, https://doi.org/10.3390/microorganisms10081510.
[43] L. Frank, M. Wenig, A. Ghirardo, A. van der Krol, A. C. Vlot, J. P. Schnitzler, M. Rosenkranz, *Plant Cell Environ.* **2021**, *44*, 1151, https://doi.org/10.1111/pce.14010.
[44] M. Ye, G. Glauser, Y. Lou, M. Erb, L. Hu, *Plant Cell* **2019**, *31*, 687, https://doi.org/10.1105/tpc.18.00569.

License and Terms

The definitive version of this article is the electronic one that can be found at https://doi.org/10.2533/chimia.2022.939