

Patterns

Chemical composition: Hearing insect defensive volatiles

Highlights

- The defensive secretion emitted by insects is often a mixture of volatiles
- Volatiles were translated into sounds by sonification using parameter mapping
- Chemical signals were repulsive for predators, as were the sounds for humans

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In brief

A methodology is described to predict and compare the interspecific repellence of defensive secretions from insects that typically emit volatiles as complex mixtures. Sonification by parameter mapping allowed us to hear single molecules, then their mixtures. Bioassays used insect predators tested against the two sets of stimuli, single and mixed volatiles, as well as humans hearing the corresponding auditory translates. The model based on gathered chemical data can serve as a proxy but quantitative indicator of repellent bioactivities.



Article

Chemical composition: Hearing insect defensive volatiles

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THE BIGGER PICTURE Insects are often defended against predators by emitting volatile secretions that act as a repellent. Chemical analyses of a secretion provide a list of compounds and their concentrations, but it then remains challenging to study their single and combined bioactivities. Here, we provide a first approach in understanding the bioactivity of single volatiles and volatile mixtures by developing a process of sonification (parameter mapping) to model chemical signals into auditory ones. Our study reveals via bioassays that foraging predators are repelled by volatiles as are human volunteers upon hearing "sonified volatiles". In these audio clips, we could also identify one sound attribute, their maximal loudness, that correlates well with the human response in the modeled world and hence with the predator response in the real world. These findings may help in exploring and understanding the seemingly overabundant diversity of deleterious chemicals present in insects and other organisms.



Development/Pre-production: Data science output has been rolled out/validated across multiple domains/problems

SUMMARY

Chemical signals mediate major ecological interactions in insects. However, using bioassays only, it is difficult to quantify the bioactivity of complex mixtures, such as volatile defensive secretions emitted by prey insects, and to assess the impact of single compounds on the repellence of the entire mixture. To represent chemical data in a different perceptive mode, we used a process of sonification by parameter mapping of single molecules, which translated chemical signals into acoustic signals. These sounds were then mixed at dB levels reflecting the relative concentrations of the molecules within species-specific secretions. Repellence of single volatiles, as well as mixtures of volatiles, against predators were significantly correlated with the repulsiveness of their respective auditory translates against humans, who mainly reacted to sound pressure. Furthermore, sound pressure and predator response were associated with the number of different molecules in a secretion. Our transmodal approach, from olfactory to auditory perception, offers further prospects for chemo-ecological research and data representation.

INTRODUCTION

Research on insect chemical ecology and evolution aims to explain the diversity of chemicals acting between species^{1,2} and often functioning as a defense against predators.³⁻⁵ Chemical diversity relates to a hierarchically structured complexity, integrating physicochemical properties of molecules, species-specific chemical profiles, and other traits related to physiology, morphology, and behavior.⁶ Each of these characteristics affects the function and effectiveness of bioactive chemicals in ecosystems. Numerous insect species produce allomones: interspecific

chemical signals beneficial to the emitter but not the receiver. Volatile allomones are secreted and emitted by epidermal exocrine glands. The chemical profile of one species can include numerous different compounds; hence the notion of a complex mixture.^{4,7,8} Analytical chemistry of a defensive secretion from a species leads to determining its chemical profile, which is basically a list of compounds and their concentrations. Although the bioactivity of each compound underlies the bioactivity of mixed compounds, the functional link between both levels remains difficult to assess.

Obviously, the bioactivity of a volatile relates to several of its physicochemical parameters.⁷ For instance, biological and



toxicological activities of volatiles as gases and vapors against mammals and amphibians can be predicted by quantitative structure-activity relationships (QSARs) and derived equations, which combine independent variables, such as excess molar refraction, dipolarity, and hydrogen bond acidity/basicity.⁹ Such data about insect allomones may not be available; for instance, because of an unresolved double bond positioning in a chemical structure. More importantly, QSARs generally refer to the bioactivity of single molecules, whereas the procedure remains problematic when considering the kinetics of complex mixtures.¹⁰ As far we know, QSARs were never applied to mixtures of many volatiles. Technical problems are also encountered when attempting to quantify the repellence of insect defensive allomones, because it requires, for example, reproducing a secretion by starting with standard volatiles and mixing them, or to collect and accumulate enough of a native secretion. This is difficult with many insect species that produce a secretion in small quantities, preventing the collection of sufficient amounts for biological testing. Moreover, many species are collected in the field where they are often rare in space and/or time.

To explore and analyze the bioactivity of volatiles involved in defense, we propose that a modeled system can be obtained by a process of sonification. This is the use of non-speech audio to convey information or percept data.^{11,12} It has already been applied in neuroscience and on chemically (mainly genomic) based datasets in domains, such as medicine and perfumery^{13–22} to study, for instance, the cross-modal perception of odors by humans.²³ Sonification is also applied, more generally, to help visually impaired people²⁴ as well as in the study of brain activity,²⁵ animal migration,²⁶ geographic data,²⁷ volcanic seismograms,²⁸ mathematical data,²⁹ internet monitoring,³⁰ and other scientific and technical areas.^{31–34} Sonification appears especially suited to the study of defensive volatiles.³⁵ Indeed, a parallel can be drawn between the perception of volatile chemicals and that of sounds. There is a similar spatiotemporal dynamic of the propagating stimuli: the high volatility of rather small molecules is transferable to a high tone frequency (pitch) and a short duration of a tone and its reverberations; the occurrence of functional groups is mirrored in the sound's timbre; and the amount of a perceived single compound, or its relative concentration within a mixture, would relate to the loudness of the sound, loudness being a perceptual quality of a sound that is linked to its amplitude. Thus, the perception of an evaporating blend could be rendered by combining the characteristics of the single components.

From an ecological point of view, it is challenging to explain the complexity of some allomonal secretions, including many different volatiles. Yet, their basic function as a repellent is to keep away walking or flying aggressors.³⁶ Some compounds of a mixture can be precursors or solvents of effectively repellent compounds,³⁷ and a defensive secretion is emitted against a range of predator species. These two aspects can partly account for the complexity of chemical profiles. Furthermore, any bioactive volatile of a defensive secretion can be assumed to be a repellent in some conditions. Dose-dependent effects of a chemical are ubiquitous, and volatiles at some concentration can attract an organism, while at a higher concentration they can become aversive for that same organism.^{7,38,39} For instance,

in a human context, even the delicate floral bouquet of a perfume may become repellent if smelled at high concentration. At an interspecific level, compounds can deter or repel generalist predators while they may be inactive or even attract specialized predators.^{40–43}

In chemical ecology, repellents can be defined as nonspecific irritants rapidly acting on the chemical senses, in contrast to specific poisons typically acting more slowly and deeply in the body.³ When a foraging predator perceives molecules via olfaction, “negative” and “positive” perceptions are generally asynchronous, whereas via gustation feeding deterrents and phagostimulant compounds are perceived concurrently. Thus, there may be a higher potential for volatiles compared with water-soluble compounds to be used in defense, because volatiles induce a predator to detect a prey before possibly subduing it. As a consequence, the prey has a higher escape probability. This may explain why so many insects are defended by volatiles.^{4,5,8} But more research is needed to elucidate the relationships between the allomonal bioactivity of a complex mixture and the one of its constituent single molecules.

Our study focuses on sawfly larvae belonging to the subfamily Nematinae (Hymenoptera: Tenthredinidae). These plant feeders generally live on leaves and are often preyed upon by insectivorous insects such as ants.⁴⁴ The anti-predator defense of most nematines relies on volatiles emitted by ventro-abdominal exocrine glands⁴⁵ that vary in size across species.⁴⁶ These pouch-like glands can be turned inside out by the larva, the secretion that they contain then starting to evaporate. The defensive secretions include compounds from one to several of the chemical classes aliphatics, aromatics, and terpenes (Figure 1). The odor of the defensive secretions is described as unpleasant for some species belonging to the genera *Nematus*, *Pristiphora*, and *Trichiocampus*.^{47,48}

This paper aims to assess whether audio files generated by sonification constitute an approximation of the bioactivity of complex defensive secretions. Our approach compared the behavioral effects of an identical set of chemical data in two unrelated perceptive worlds, smelling versus hearing. We tested in the “real world” the repellence of single and mixed volatiles against predatory ants; while, in a “modeled world,” we tested the sonified translates of single molecules and chemical profiles against humans. As well as chemical parameters, other factors potentially affecting the efficiency of a chemical defense were integrated in our study. We were able to validate the starting hypothesis that, for both single molecules and mixtures, determinants of repellence can be accessed via sonification.

RESULTS

Ant response to single volatiles versus live prey insects defended by volatiles

Twenty single standard compounds were tested for their repellence against ant workers (Table 1; experiment 1). Absolute amounts of evaporated molecules were measured using the same standards (dataset 1). Ant response was not correlated with the quantity of evaporated molecules (Table 1; Figure 2). The total number of functional groups present in a molecule was associated with the ant response ($p < 0.005$, Spearman



Figure 1. Volatiles detected in the glandular secretion of the studied nematine species

Volatiles were detected and identified by gas chromatography-mass spectrometry of dissected ventral glands, following references for the genera *Cladius*,⁴⁸ *Craesus*,⁶¹ *Hoplocampa*,⁵⁷ and *Nematus*.⁶⁰ The left part of the figure is continued on the right part. The values with colored backgrounds express large (4), medium (3), small (2), or trace amounts (1) in the respective species. The volatiles are grouped per chemical class (aliphatic, aromatic, or terpene) and sorted in increasing order of molecular weight. Further details about the molecules are given in Table S1, in which the chemical data were compiled from standard works.^{66–68}

rank-order correlation test; N = 20 molecules, experiment 1 and corresponding data from Table S1).

Live nematine larvae were confronted with foraging ants and the number of ants around a larva was counted (experiment 2; Data S1). In this bioassay setup, the number of ants is an inversely proportional measure of the defensive effectiveness of the sawfly. The defensive efficiency of nematine larvae was significantly and positively correlated with the number of different compounds detected in their glandular secretion (Table 2; Figure 2). The gland size measured from the sawfly larvae (dataset 2) was also positively correlated with defensive efficiency (Table 2; Figure 2). In contrast, gland size was not correlated with the number of different molecules detected in a glandular secretion (Table 2; Figure 2).

The process of sonification

The sonification was achieved as follows. We converted physicochemical descriptors of single volatiles (Figure 1) into sounds by parameter mapping,⁴⁹ which required the use of a sound synthesizer. A different preset of the synthesizer was assigned to each chemical class. Both assignment and parameter mapping were performed in a semi-empirical way to gather output sounds: (1) that were distinctive between the three chemical classes encountered in the glandular secretions and (2) that varied in their perception depending on chemical characteristics. Note that such chosen settings are required in the course of any sonification process.^{16,17,19,20,22,49,50} The settings first tried by using a few molecules from each chemical class were then identically processed on all molecules. For molecules occurring

Table 1. Results from experiments and datasets involving single molecules

Compound	Experiment 1: ant response (% repelled by volatile)	Dataset 1: quantity evaporated (10^{-7} moles)	Experiment 3: human response (% repelled by audio)	Dataset 4: Lpeak (dB)
Methanol	26.3 ± 4.6	139	44 ± 18	-23
Formic acid	93.6 ± 7.4	383	35 ± 19	-16
Ethanol	6.0 ± 1.0	204	40 ± 19	-22
Acetic acid	77.7 ± 13.3	303	39 ± 20	-16
Pentane	12.1 ± 0.5	0	28 ± 18	-33
Hexane	7.1 ± 10.1	3	28 ± 17	-31
(E)-2-Hexenal	97.8 ± 3.1	157	91 ± 17	-5
(E)-2-Hexen-1-ol	83.4 ± 8.2	100	49 ± 22	-16
Hexanoic acid	56.2 ± 7.4	3	33 ± 17	-21
Octan-1-ol	82.4 ± 9.9	19	55 ± 24	-14
Hexadecanoic acid	3.5 ± 6.8	1	34 ± 20	-22
Toluene	38.9 ± 8.2	74	31 ± 19	-27
Benzaldehyde	96.9 ± 4.3	76	56 ± 23	-12
2-Hydroxybenzaldehyde	97.7 ± 2.7	32	84 ± 17	0
(-)- α -Pinene	73.6 ± 9.0	111	26 ± 17	-35
D-Limonene	88.4 ± 7.7	70	26 ± 16	-35
α -Terpinene	91.5 ± 7.6	86	25 ± 15	-35
Myrcene	74.0 ± 12.4	19	27 ± 17	-35
Geranial	92.4 ± 2.2	4	53 ± 20	-16
Neral	92.4 ± 2.2	4	55 ± 22	-16

For complementary data about the compounds, see [Table S1](#). The compounds are sorted by chemical class, then by increasing molecular weight. Mean ± standard deviation, or absolute values are shown. Experiment 1: maximum percentage of *Crematogaster scutellaris* ant workers repelled by 0.25 μ L of an evaporating volatile, during 4.5 min from $t = 30$ s to 5 min. Dataset 1: quantity of 2.5 μ L volatile evaporated during 4.5 min from $t = 30$ s to 5 min. Experiment 3: percentage of the distance walked backward by volunteers relative to the individual maximum distance reached throughout the experiment of hearing molecule audio files. Dataset 4: peak sound pressure measured from the audio file obtained by sonification of a molecule. See [supplemental information](#) for raw data, and [experimental procedures](#) for further explanation.

in glandular secretions, the sounds were finally mixed up at sound pressure levels following their relative abundance in the insect species as calculated by gas-chromatographic analyses (see [Figure 1](#)). Thereafter, 20 molecule audio files and 16 species audio files were tested for their auditory repulsiveness against human volunteers by measuring the distance the volunteers walked backward upon hearing these files (experiments 3 and 4, respectively). In other words, the maximum distance reached by each volunteer was determined. Then the distance upon hearing each of the audios was divided by individual's maximum distance and expressed as a percentage. Finally, these percentages were averaged over all volunteers.

Human response to audio files of sonified single molecules and glandular secretions

While being tested for the series of 20 single molecules (experiment 3), most volunteers evoked unpleasant features of some sounds, mainly loudness and especially high-pitched sounds, to explain their walking backward. They also often mentioned that each audio clip with a longer lasting climax would have allowed them to better adjust the distance they walked backward. The audio files corresponding to the secretion of the 16 species were therefore played twice: the first time immediately followed by a second time, the distance between the loudspeakers and the volunteer was measured at the end of the second playing (experiment 4). Nevertheless, some volun-

teers commented again that it was difficult to exactly position themselves due to the shortness of some sound sequences.

The quantitative results of testing single molecules and glandular secretions against ants (experiments 1 and 2) and testing their auditory translates against humans (experiments 3 and 4) revealed that ant and human responses are correlated when testing single molecules as well as mixtures ([Tables 1, 2, and 3](#); [Figure 2](#)). Furthermore, the human response against single molecules was not correlated to the quantity of evaporated molecules. For mixtures of volatiles, the correlations were significant between the number of different molecules identified in a secretion and both the responses by ants and those by humans. Across nematine species, gland size was more strongly correlated with ant response than it was with human response ([Table 3](#); [Figure 2](#)).

Sound pressure of the audio files

Following the comments by human observers that they were particularly repulsed by loud sounds, we decided to calculate the peak sound pressure (Lpeak) from all tested audio files (datasets 4 and 5). This Lpeak was highly correlated with human response for both single molecules and mixtures ([Table 3](#); [Figure 2](#)). As for human response, Lpeak was also significantly correlated to ant responses and the number of different molecules in the secretion, whereas it was also not correlated to the quantity evaporated ([Table 3](#); [Figure 2](#)).

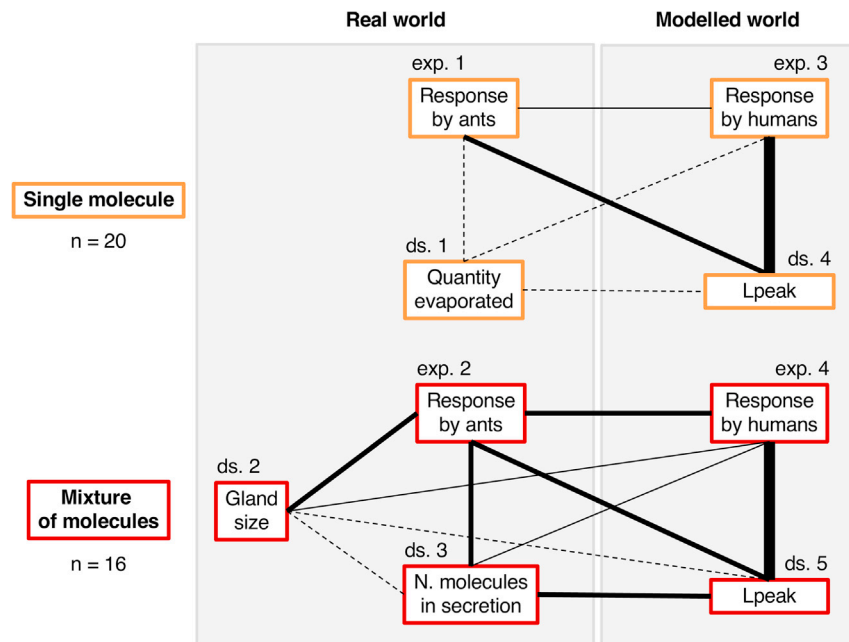


Figure 2. Schematic representation of statistical correlations between bioassay experiments and related datasets

Both perceptive worlds, the real chemical one and the modeled auditory one, are based on an identical set of chemicals (Table S1). In the real world, the repellence of single volatiles (exp. 1) and the defensive efficiency of prey species using volatiles as defense (exp. 2) were tested against ants. In the modeled world, sonified single molecules (exp. 3) and sonified prey defensive secretions (exp. 4) were tested for their repulsiveness against human volunteers. Spearman rank-order correlations were then calculated between these responses by ants and humans, plus other datasets not gathered from bioassays: evaporated quantity of single molecules (ds. 1); size of the defensive glands of the prey species (ds. 2); number of molecules occurring in the glandular secretion of the prey (ds. 3); and maximum peak reached by the sound pressure, L_{peak} , as measured from the audio files tested on human volunteers (ds. 4 and 5). The statistical significance of the correlation between these variables by Spearman rank-order correlation tests is represented by the type of line linking them: $p > 0.05$ (dashed line), $p < 0.05$, $p < 0.01$, $p < 0.001$ (thin to thick line, respectively). Exact significance levels are given in Table 3.

Alternative mapping

A topic still not addressed is alternative mapping conditions. So far, a single mapping condition was applied on all molecules, subsequently leading to the experiments and datasets of the model as well as to most of the correlation calculations (Figure 2). This mapping was selected by semi-empirical choices at the levels of synthesizer presets and the parameter mapping itself. The synthesizer includes over 1,300 presets, and each one can be customized by numerous detailed settings of oscillators, filters, reverbs, etc. Three presets were selected and assigned to the three chemical classes (see experimental procedures). The mapping itself specifically linked eight chemical parameters to nine sound parameters, thus using one mapping configuration with nine mapping nodes, although a multitude of such configurations are conceivable. Less or more chemical and sound parameters could theoretically have been included and linked. Thus, overall, there is a virtually infinite number of possible combinations in the general process of choosing a synthesizer preset and of parameter mapping. Our assumption was that an “audio-guided” selection of mapping conditions would be more efficient than if determined at random to adjust the modeled audios to the experimental data with ants.

To assess this assumption, 24 alternative conditions were randomly applied on part of the mapping settings, with the aim of correlating ant responses with L_{peak} values of the 20 single molecules (see Table 1). The results from this screening revealed that 17 correlations were less significant than when using the mapping that led to dataset 4, whereas of the 7 other comparisons, the most significant p value reached <0.001 (Table 4).

DISCUSSION

Ant responses

As with many other chemically defended insects, nematine larvae emit their glandular secretion only when they are

disturbed. This indicates a defensive function of the secretion, and indeed larvae with experimentally emptied glands are strongly attacked by ants.⁴⁶ Our results indicate that the ant response to standard volatiles is determined by factors other than the evaporation rate. The association between the total number of functional groups and ant response also indicates that any functional group seems to impact ant response by its presence alone, regardless of its nature as acid or aldehyde group, etc. But, although a chemical defense acts along with other traits such as defensive behavior,^{4,46} the ant response to mixtures was correlated with the number of volatiles in the glandular secretion, suggesting that chemical diversity by itself increases the bioactivity of a mixture. This is in agreement with the integrated chemical defense hypothesis postulated for insect-plant interactions.⁵¹ Since ant response was also correlated with the gland size of the nematine larvae, it seems that their defensive efficiency is proportional to the amount of glandular secretion emitted. However, the fact that the species-specific chemical diversity of the secretion was uncorrelated with the size of the glands may indicate that gathering a complex chemical profile is not influenced by the chemical analyses themselves and that would detect fewer compounds in small glands than in larger ones.

Human responses

Interestingly, some volunteers commented that the shortness of several sound sequences prevented them from adjusting their “comfort position” upon hearing these sequences. Placed in the real-world context, these comments can be interpreted by considering that defensive volatiles need to act as rapidly as possible, and that their efficiency is never too high. Indeed, from the point of view of a prey, such as a nematine larva, its defensive secretion should keep a potential aggressor as far away as possible; while, from the point of view of the predator,

Table 2. Results from experiments and datasets involving mixtures of molecules

Species	Experiment 2: ant response (no. of ants)	Dataset 2: gland size (0.01 mm ²)	Dataset 3: no. of molecules	Experiment 4: human response (% repelled by audio)	Dataset 5: Lpeak (dB)
<i>Cladius grandis</i>	2.2 ± 1.5	7 ± 2	26	22 ± 23	−15
<i>Cladius pectinicornis</i>	1.0 ± 1.1	2 ± 1	18	16 ± 23	−20
<i>Craesus alniastri</i>	1.0 ± 1.6	27 ± 2	10	31 ± 28	−16
<i>Craesus latipes</i>	0.3 ± 0.3	42 ± 12	13	36 ± 32	−16
<i>Craesus septentrionalis</i>	0.8 ± 0.9	43 ± 9	14	40 ± 38	−15
<i>Hoplocampa testudinea</i>	0.0 ± 0.0	26 ± 8	28	90 ± 15	−2
<i>Nematus lucidus</i>	11.1 ± 3.7	7 ± 1	9	9 ± 15	−20
<i>Nematus melanocephalus</i>	6.4 ± 3.5	4 ± 0	2	10 ± 16	−29
<i>Nematus miliaris</i>	0.5 ± 0.3	16 ± 1	10	26 ± 24	−14
<i>Nematus nigricornis</i>	6.1 ± 2.5	–	8	31 ± 27	−16
<i>Nematus papillosus</i>	0.3 ± 0.7	29 ± 4	20	75 ± 24	−7
<i>Nematus pavidus</i>	0.1 ± 0.2	41 ± 11	22	70 ± 27	−8
<i>Nematus salicis</i>	5.3 ± 3.9	3 ± 2	9	36 ± 23	−15
<i>Nematus spiraeae</i>	0.1 ± 0.1	36 ± 10	18	52 ± 32	−12
<i>Nematus tibialis</i>	4.5 ± 0.4	3 ± 1	4	24 ± 25	−18
<i>Nematus viridissimus</i>	3.5 ± 1.7	10 ± 6	23	71 ± 27	−7

The listed species are detailed in [Figure 1](#). Mean ± standard deviation, or absolute values are shown. Experiment 2: number of *Myrmica rubra* ant workers surrounding a larva. Dataset 2: surface of ventral glands. Dataset 3: total number of different molecules identified in the glandular secretion, see [Figure 1](#). Experiment 4: percentage of the distance walked backward by volunteers, relative to the individual maximum distance reached throughout the experiment of hearing species audio files. Dataset 5: peak sound pressure measured from the audio file obtained by sonification of the glandular secretion of a species. Not measured (–). See [supplemental information](#) for raw data, and [experimental procedures](#) for further explanation.

its position relative to the prey item will be a continuous balance between its quest for food and its confrontation with the volatiles.

Both human and ant responses against single molecules were not correlated to the quantity of evaporated molecules, suggesting that human response is in accordance with ant response. The unrelatedness between human response and quantity of evaporated molecules is explained by the fact that the sonification used molecule attributes, such as the occurrence of functional groups, not physicochemical data such as vapor pressure and boiling point. These latter descriptors are more directly related to the physical process of evaporation, but from a practical standpoint they remain quite often unknown for at least one-third of the molecules detected in the studied secretions (estimation from own data sources). Moreover, the fact that a compound, such as 2-hydroxybenzaldehyde, weakly evaporates but is highly repulsive against humans as well as ants, indicates that the aforementioned unrelatedness is not attributable to the sonification process itself. Across nematine species, gland size was less strongly correlated with human response than it was with ant response. A reason for this may be that gland size is a trait not included in our sonification process, while it influences the ant response in the real world as far as the amount of a secretion is proportional to gland size.

Quantity and quality of volatiles

We are aware that volatile amounts were only considered while mixing compounds to obtain audio files of species. Since gland sizes vary from one species to another, the overall amount of

produced secretion is certainly also species specific. But, within a species, it is virtually impossible to determine during predator-prey interactions which portion of the secretion is evaporating from the prey, and which vapor concentration is perceived by the predator. The dynamic of such interactions implies continuous spatiotemporal changes at these levels of secretion emission and perception. Conversely, the chemical profile of a secretion remains more constant. This was therefore used here in building the species audio files, being independent of the overall amount of secretion produced, emitted, and ultimately perceived.

We did not evaluate the possibility that sounds might be attractive to the listeners. Similarly, ants were only tested for negative behavioral responses to volatiles and live prey insects. Thus, the receiver organisms, ants and humans, could either move away from the signal source, which we then interpreted as being repulsive, or remain close to it. The latter situation may indicate either a positive or neutral non-response. But, in any case, the goal of our study was to focus on an interspecific comparison of insect secretions obviously used in defense, which undoubtedly does not exclude the fact that some of their compounds may play other roles in other ecological circumstances.⁵²

Sound pressure of the audio files

Real-world bioassays using ants and prey species provide valuable behavioral observations of predator-prey interactions, because ants are confronted with both a live prey item and its emitted defensive secretion. In contrast, the strong correlation between human response and Lpeak values indicates that using such a sound measurement may be more convenient and accurate, thus appropriate

Table 3. Statistical significance of correlations across experiments and datasets involving single molecules and mixtures of molecules

		n	r_s	t	df	p
Single molecule						
Experiment 1	dataset 1	20	0.2944	1.31	18	0.207
Experiment 1	experiment 3	20	0.5041	2.48	18	0.023
Experiment 1	dataset 4	20	0.5807	3.03	18	0.007
Dataset 1	experiment 3	20	0.1526	0.66	18	0.518
Dataset 1	dataset 4	20	0.1684	0.73	18	0.475
Experiment 3	dataset 4	20	0.9391	11.6	18	<0.001
Mixture of molecules						
Experiment 2	dataset 2	15	-0.7049	-3.58	13	0.003
Experiment 2	dataset 3	16	-0.6773	-3.44	14	0.004
Experiment 2	experiment 4	16	-0.6982	-3.65	14	0.003
Experiment 2	dataset 5	16	-0.6845	-3.51	14	0.003
Dataset 2	dataset 3	15	0.3498	1.35	13	0.200
Dataset 2	experiment 4	15	0.5989	2.7	13	0.018
Dataset 2	dataset 5	15	0.4762	1.95	13	0.073
Dataset 3	experiment 4	16	0.6111	2.89	14	0.012
Dataset 3	dataset 5	16	0.7469	4.2	14	0.001
Experiment 4	dataset 5	16	0.8873	7.2	14	<0.001

By Spearman rank-order correlations, the two-sided p values (p) are given in bold when statistically significant, at $\alpha = 0.05$, after false discovery rate control. Sample size (n), Spearman's correlation coefficient (r_s); size of difference relative to variation in the sample data (t); degrees of freedom (df). Variables and sample data refer to Tables 1 and 2; see Figure 2 for an illustrated summary of the statistics.

than testing audio files to quantify the repellent effect of a molecule or secretion in the modeled world. Indeed, human response and Lpeak were closely related representatives of the modeled world, and both similarly reflected the real one.

Sound strength was not explicitly involved in parameter mapping, although it is influenced by parameters, such as pitch and timbre; however, this was directly involved when mixing molecule audio files into a species audio file. Thus, a surprising result is its correlation with ant response even for single molecules. This suggests that molecule characteristics were adequately revealed by parameter mapping, even if the process was partly empirical and involved quite basic chemical descriptors. Our results are coherent also from a chemo-ecological point of view in that Lpeak values from the species audio files were correlated with the level of complexity of the corresponding chemical profiles. More generally, the sonification of single molecules and chemical profiles leads to subtle audio files that render the diversity and perceptive richness existing within and across volatile mixtures. In this respect, a complementary analysis of each audio file could be done by extracting other sound properties than loudness, such as its harmonic complexity or predominant frequencies. Note that, in a first approach, such attributes are viewable in the spectrogram, or sonogram, of an audio by using an appropriate sound software.

Alternative mapping and further research directions

Testing alternative mapping conditions revealed that the mapping initially chosen in this study to perform the bioassays on

humans and to gather the sound pressure datasets conveyed sufficient accuracy from the real world to the modeled world. Yet, it may be worth combining empirical with randomized approaches when searching for the most effective mapping conditions to further enhance the precision of the modeled system.

We observed some trends in the effect of attributing functional groups to sound parameters because given chemical-sound mapping conditions tended to specifically increase or decrease the statistical significance. Nevertheless, it remains difficult to understand the causal relationship between the mapping conditions and the subsequent statistical results from comparing data from Lpeak with those from ant responses. Parameter mapping thereby resembles a process, such as machine learning, by which data patterns are obtained in a non-predetermined way.⁵³ Machine learning is considered as a potential tool in the search of linking chemical attributes with the identification of human microbial pathogens based on their volatiles.⁵⁴ Similarly, our data could theoretically also be analyzed by a neuronal network trained on chemical parameters to provide predictive ant responses as output. We consider, however, the sonification process as a useful approach complementary to QSAR or machine learning because it can handle small datasets and because the data integrated in the modeled world can be perceived by hearing. Hence, the biological perception by us versus predators allows a "dual bioguided" development of the model. Furthermore, the sonification of single volatiles and mixtures may be used not only in chemo-ecological research, but also in chemical data representation and science education,^{18,50} but see Supper.⁵⁵

At a practical level we are aware that, since the core tests were performed several years ago (on a MacOS computer), some software versions related to the codes developed in the present study may be outdated, as follows (see also [sonification](#), under [experimental procedures](#)). First, one should use Processing v.2 as we noticed that v.3 poses a problem with associated libraries. But it should be quite easy to adapt the codes to the latest version. Second, one may get slightly different sounds when using the latest version of Massive (currently Massive X) compared with its v.1, although both versions, X and 1, remain downloadable. Third, we suggest an alternative for the outdated software SoundFlower that can be substituted by BlackHole.

In the chemical ecology of defensive allomones, there is also a question about how to adjust the sonification methodology to other predator-prey systems. In particular, the predators may be invertebrates other than ants or even vertebrates, and the chemical profile from a given prey taxa may include other and/or supplementary chemical classes than those described in the defensive secretions of nematodes. Our view is that a sonification process can be launched once bioactivity data are gathered from testing even a small set of chemical standards on a predator. Parameter mapping should start by adapting the chemical and sound parameters to be considered in ways similar to the alternative mapping described here and that especially focused on the mapping of functional groups. Note that our alternative mapping used the same chemical class of the aliphatics for all 20 molecules. This indicates that the presence of functional groups is more important than the chemical class to which a molecule belongs in determining its repellence against predators. Applying the optimized mapping conditions on the

Table 4. Statistical significance of correlations between experiment 1 and LPeak datasets from alternative, random mapping conditions

Mapping	ac	al	db	ol	rS	t	p
Set07	EQ-Boost	feedback	Clip-DW	modulation	0.7207	4.41	<0.001
Set17	Clip-DW	feedback	EQ-Boost	noise	0.7032	4.2	0.001
Set20	HP-Reson	feedback	noise	modulation	0.6664	3.79	0.001
Set21	HP-Reson	feedback	EQ-Boost	modulation	0.6335	3.47	0.003
Set22	HP-Reson	feedback	EQ-Boost	Clip-DW	0.6267	3.41	0.003
Set03	feedback	EQ-Boost	noise	Clip-DW	0.6252	3.4	0.003
Set23	HP-Reson	feedback	Clip-DW	modulation	0.6091	3.26	0.004
[Original]	noise	feedback	HP-Reson	EQ-Boost	0.5896	3.1	0.006
Set14	modulation	feedback	noise	EQ-Boost	0.5422	2.74	0.013
Set24	HP-Reson	noise	feedback	modulation	0.5379	2.71	0.014
Set05	feedback	Clip-DW	noise	modulation	0.5285	2.64	0.017
Set01	feedback	noise	modulation	Clip-DW	0.527	2.63	0.017
Set02	feedback	noise	HP-Reson	Clip-DW	0.5083	2.5	0.022
Set19	Clip-DW	EQ-Boost	HP-Reson	noise	0.4768	2.3	0.034
Set12	noise	Clip-DW	HP-Reson	modulation	0.4586	2.19	0.042
Set18	Clip-DW	feedback	modulation	noise	0.4368	2.06	0.054
Set09	EQ-Boost	<i>modulation</i>	noise	<i>HP-Reson</i>	0.3481	1.58	0.132
Set04	feedback	<i>modulation</i>	noise	Clip-DW	0.3384	1.53	0.143
Set10	EQ-Boost	<i>modulation</i>	Clip-DW	<i>HP-Reson</i>	0.3308	1.49	0.154
Set08	EQ-Boost	<i>modulation</i>	noise	Clip-DW	0.2841	1.26	0.224
Set06	feedback	HP-Reson	noise	Clip-DW	0.2382	1.04	0.312
Set16	modulation	Clip-DW	HP-Reson	EQ-Boost	0.1928	0.83	0.417
Set11	EQ-Boost	<i>modulation</i>	Clip-DW	noise	0.1858	0.8	0.434
Set15	modulation	Clip-DW	noise	<i>feedback</i>	0.1003	0.43	0.672
Set13	EQ-Boost	Clip-DW	modulation	noise	0.0372	0.16	0.875

As well as the 24 randomly selected mapping conditions (set), the original mapping is also given. This mapping was used in experiments 3 and 4 as well as datasets 4 and 5. The four chemical parameters are: acid group (ac), aldehyde group (al), double bond (db), and alcohol group (ol). The mapping data are sorted in decreasing order of statistical significance. For each chemical parameter, some sound parameters were present only in mapping combinations leading to significant p values (in bold) or non-significant p values (in italic). Statistical results are from Spearman rank-order correlations, as detailed in Table 3, but without applying a false discovery rate control.

chemical profiles from prey species shall ultimately lead to estimating and comparing across these species the repellent efficiency of their defensive secretion.

Concluding remarks

Our transmodal modeling from insect defensive chemical mixtures to audio outputs revealed a match between the repellence of these chemicals against predators and the repulsiveness of the auditory translates to humans. A crucial methodological point is that the bioassays with humans mimicked those testing the repellence of single molecules and glandular secretions against ants, by measuring how both test organisms literally moved away from a chemical versus audio source. Our transmodal approach was limited to the study of allomones and probably would not be useful in studies, for instance, of pheromones; unlike defensive secretions, pheromones act intraspecifically. Thus, our results show that, for allomones, a *trans*-modality of perceptual responses is possible from a chemical to sonic world, leading to statistically significant correlations between variables coming from both domains. The sonification procedure, coupled with Lpeak measurements, provides insights into the bioactivity

of defensive secretions by merely relying on chemical profiles, even if few bioassays on predator-prey interactions can be performed. Sonification may be one of the tools⁵⁶ to examine the intra- and interspecific chemical diversity of insect volatiles occurring in mixtures.

Sonification is often used to bridge two unrelated domains in order to apprehend a complex phenomenon, the sonic domain being created to gather a better knowledge of the one on which it is based. Following our starting hypothesis that determinants of repellence can be accessed via sonification, the results obtained by comparing prey species indicate that the complexity of a mixture may be one of such determinants. Moreover, the sonification allowed us to get a new perception of the bioactivity of defensive secretions by hearing it, and to quantify this perception by measuring the sound intensity. Direct comparisons were more convenient with sound pressure values than results from testing humans because the latter data were more difficult to obtain. Further research may evaluate the sonification model in the context of other biological systems involving single volatiles and preferably mixtures of volatiles, to better understand the ecological importance of a chemical composition.

EXPERIMENTAL PROCEDURES

Resource availability

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Jean-Luc Boeve (jean-luc.boeve@naturalsciences.be).

Materials availability

The audio clips of the 20 molecules (Table 1) and 16 species (Table 2) are available as MP3 files from Freesound: <https://freesound.org/people/jlboeve/packs/30377/>.

Data and code availability

The datasets generated during the study are available in Data S1. The three NMSV files are proprietary algorithms and available on request. The PDE codes are available in Data S2. The methodologies described in the following subheadings are related to the real world (i.e., experiments 1 and 2; datasets 1, 2, and 3) and the modeled one (sonification, experiments 3 and 4; datasets 4 and 5). Part of the original data related to experiments 1, 2, and 3, and dataset 2 refers to the literature.^{35,46,57}

Insect material

The larvae of nematine sawfly species were collected in the field. They were identified following Lorenz and Kraus⁴⁷ and their nomenclature followed Taeger et al.⁵⁸ The studied species are: *Cladius grandis* (Serville, 1823) (formerly *Trichocampus viminalis* [Fallén, 1808]); *Cladius pectinicornis* (Geoffroy, 1785); *Craesus alniastri* (Scharfenberg, 1805) (formerly, genus *Craesus* and species *C. varus* [Villaret, 1932]); *Craesus latipes* (Villaret, 1832); *Craesus septentrionalis* (Linné, 1758); *Hoplocampa testudinea* (Klug, 1816); *Nematus lucidus* (Panzer, 1801); *Nematus melanocephalus* (Hartig, 1837) (formerly *N. melanocephala*); *Nematus miliaris* (Panzer, 1797); *Nematus nigricornis* (Serville, 1823); *Nematus papillosus* (Retzius, 1783) (formerly *N. melanaspis* [Hartig, 1840]); *Nematus pavidus* (Serville, 1823); *Nematus salicis* (Linné, 1758); *Nematus spiraeae* (Zaddach, 1883); *Nematus tibialis* (Newman, 1837); and *Nematus viridissimus* (Möller, 1882). Species were not selected on the basis of their phylogenetic relationships, but to include in the study a qualitative and quantitative variety of chemical profiles. Voucher specimens are kept in the Royal Belgian Institute of Natural Sciences. The larvae were reared in boxes by providing them with fresh leaves of their host plant. They were used when full grown.

Ant colonies collected in the field were kept in the laboratory, the ant workers being fed sugar and protein sources ad libitum.

Bioassay with ants (experiment 1)

To quantify the repellence of volatiles (see Table S1), 40 ant workers of *Crematogaster scutellaris* (Olivier, 1792) were isolated from the colony and left for 30 min in an open 14 cm diameter Petri dish coated on its inner border with a polytetrafluoroethylene liquid to prevent them from escaping. An attractant of 75 μ L of a 1:1 water/honey solution was deposited on a 5 \times 5 cm glass plate with a metallic podium (diameter 1 cm, height 0.5 cm) fixed at its center, the solution was around the podium. The plate was placed in the Petri dish and the ants were allowed to find and feed on the solution for 5 min (Figure 3). The number of feeding ants was then counted for a first time ($t = 0$) while simultaneously placing on the podium a piece of 5 \times 5 mm filter paper embedded with 0.25 μ L of the tested volatile. The number of feeding ants was counted again at $t = 30$ s and each minute from $t = 1$ –5 min (Figure 3). Thus, the experimental setup prevented a direct contact between ants and a volatile, except by its vapors. The experiment was performed at 25°C and replicated two to four times per volatile, the tested ants being replaced by new ones from the colony in each replication.

The ant response to each volatile was calculated as equal to 100 minus the lowest mean ratio, in percent, of a number of feeding ants counted between $t = 0.5$ and $t = 5$ min, to the number at $t = 0$; the standard deviation (SD) was calculated on the data corresponding the lowest mean at that given time point of lowest mean ratio. A control using no filter paper and volatile yielded a repellence mean \pm SD = 7.4% \pm 2.1%. Note that in experiment 1 and dataset 1, the isomers geranial and neral were not used separately but as a racemic mixture, thus leading to identical results.

Evaporation rate (dataset 1)

Evaporation rate was measured twice per standard volatile, by impregnating a 16 \times 16 mm filter paper with 2.5 μ L volatile, then immediately depositing this paper on an analytical balance (readability: 0.01 mg; Mettler AE163, Mettler-Toledo, Leicester, UK), and weighting it at $t = 30$ s and 5 min. The weight difference quantified the volatile evaporation that was expressed in 10^{-7} moles and averaged on the two repetitions.

Bioassay with ants (experiment 2)

To test the defensive efficiency of a species-specific glandular secretion, single nematine larvae were tested against *Myrmica rubra* (Linnaeus, 1758) ant workers isolated from a colony. In field conditions, *M. rubra* and sawfly larvae can be sympatric (J.-L.B. personal observation). This ant species was used in a laboratory bioassay because it was more prone than *C. scutellaris* (used in experiment 1) to attack prey items. Yet, both ant species are generalists, feeding on carbohydrate and protein sources. Moreover, volatiles tested against different ant species generally lead to similar levels of repellence.⁵⁹

Twenty workers were placed in an open 10 \times 10 cm box having a plaster bottom. After ca. 20 min, one sawfly larva was placed at $t = 0$ in the box while avoiding any immediate contact with ants. From $t = 2$ to 5 min, the number of ants surrounding the larva was counted each 20 s, by considering those ants contacting the larva with their body, not only antennae. The experiment was replicated 3–6 times per nematine species, the tested ants being replaced by new ones from the colony in each replication. The ant response was calculated by averaging the number of ants over the 10 time points, using these values to calculate the mean \pm SD per species.

Glandular surface (dataset 2)

Larvae were stored in a fixative (ethanol, formaldehyde, acetic acid) solution before being placed in 70% ethanol. They were dissected in 70% ethanol to isolate as far as possible five ventral glands (from abdominal segments 2–6), which were then stained with Mayer's hemalum, dehydrated, and embedded in Canada balsam under a coverslip. Since each ventral gland is a flat structure,⁴⁶ half of its secretory surface was measured, using a binocular microscope, and expressed in 0.01 mm². It was often impossible to correctly dissect and measure all glands from a larva, due to their minute size, or because they were turned inside out upon fixation. The gland size of a species was calculated and averaged on 2–15 glands from 2 or 3 larvae, except on 40 glands from 10 larvae of *N. pavidus*.

Number of molecules in secretion (dataset 3)

The number of identified molecules occurring in the glandular secretion of each nematine species refers to Figure 1.

Sonification

Sounds were generated with the synthesizer Massive v.1.5.1 (Native Instruments, Berlin, Germany). We assigned to each chemical class of the aliphatics, aromatics, and terpenes an NMSV preset sound close to three available in Massive: "Cloud N9," "Diagrammatic," and "Cliff," respectively. To perform the sonification of single volatiles, CSV files contained their chemical descriptors (as tabulated in Table S1) that were linearly scaled to fit MIDI norms and translated into sound characteristics by a process of parameter mapping.⁴⁹ The mapping initially used Max/MSP (Cycling '74, San Francisco, CA, USA) to which the Massive-generated sound sequences were routed by the virtual audio bus SoundFlower to record AIF audio files individually. Later, an application was written in Processing v.2.2.1 (Processing Foundation, MIT Media Laboratory, MA, USA) (Data S2) to allow a more convenient mapping and a batch recording of WAV sounds via the virtual audio driver BlackHole v.0.2.9.

Parameter mapping was prototyped with a few volatile molecules from each chemical class. The mapping was then identically processed on each of the molecules listed in Table S1 (see Figure 4). A negative correlation was set between the number of carbon atoms (2–29) and note pitch (MIDI note range 108–33) as well as equalizer frequency (MIDI control 127–0). Positive correlations were set between the following chemical and sound parameters: molecular weight (32–425) and note duration (1–10 s); aldehyde group (0–2) and feedback amplitude (MIDI control 0–127); acid group (0–1) and noise metallic amplitude (MIDI 0–127); alcohol group (0–1) and equalizer boost (MIDI 0–64); ketone (0–1) and modulation oscillator filter FM (MIDI 0–127); ester

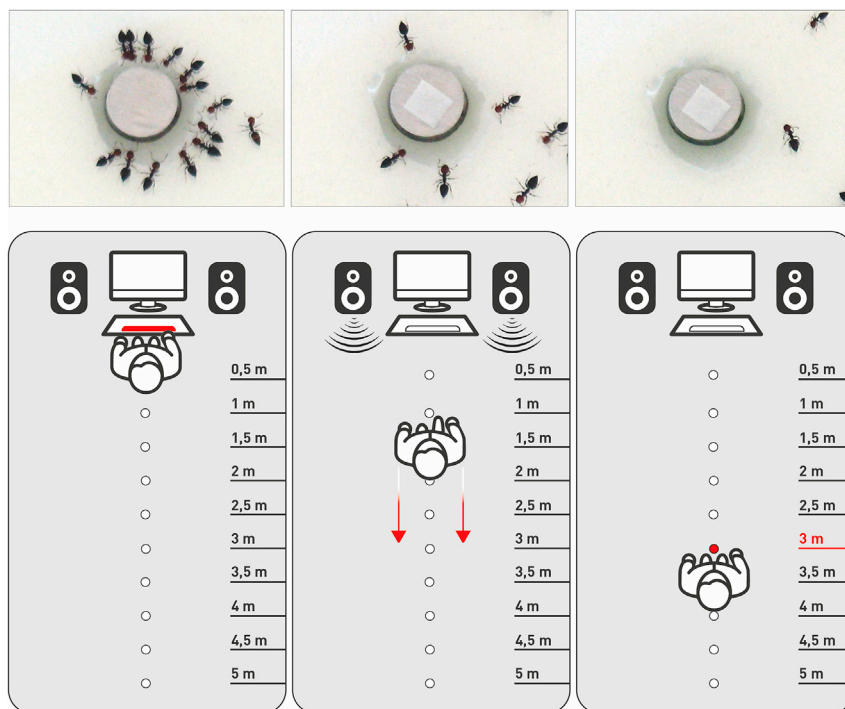


Figure 3. Illustrations of the bioassays with ants (experiment 1) and humans (experiments 3 and 4)

The three pictures (above, from left to right) were taken just before $t = 0$, and at $t = 1$ min and $t = 5$ min, respectively; they show the metallic podium surrounded by a water/honey solution, the piece of filter paper embedded with a volatile, and the ants *Crematogaster scutellaris*. The schematic diagrams (below, from left to right) represent a volunteer in the experimental environment at three typical moments of testing a sound. For more explanation, see text.

A group of 36 persons (mean \pm SD age: 25 ± 4 years) participated in experiment 3, and 27 (26 ± 4 years) in experiment 4. Each individual heard in succession the 20 or 16 audio files in a random order. The human response to the auditory repulsiveness of a given sonified molecule or mixture of molecules was calculated as the mean ratio in percent of the distance traveled by a person upon hearing an audio file to the maximum distance traveled by this person in the experiment. An example would be 36 persons all walking backward a maximum of 4 m upon hearing 20 different audios. If upon hearing a given audio

18 persons reached 2 m and the other 18 persons 4 m, the auditory repulsiveness for this audio would then be of 75%.

(0–1) and insert 1 hardclipper dry/wet (MIDI 0–127); and double bonds (not linked to functional groups; 0–3) and filter 2 highpass 4 resonance (MIDI 80–127).

The parameter mapping resulted in molecule audio files corresponding to the 20 molecules used in experiment 1, and/or to the 106 molecules occurring in the glandular secretion of at least one studied insect (Figure 1). The audio files lasted from 7 to 24 s, although most of them included a quite long, near-silent tailing (e.g., Data S3).

In the literature about the chemical profiles of the studied nematine secretions, volatile amounts are given for *Cladius* and *Nematus* species as percentages of the total secretion,^{48,60} and for *Craesus* and *Hoplocampa* species as large, medium, small, or trace amounts.^{57,61} Percentages were categorized from large to trace amounts: >15%, 6%–15%, 1%–5%, and <1%, respectively. Species audio files were then created by mixing molecule audio files in Max/MSP, the molecule files starting simultaneously. Thus, for the nematine species used in experiment 2, each of the four categorized amounts (as given in Figure 1) was assigned to a sound pressure level of 0.0, –3.8, –9.4, or –16.0 dB, respectively. This resulted in 16 audio files corresponding to as many species-specific chemical profiles of the insect glandular secretions. The audio files lasted from 19 to 25 s (e.g., Data S3).

Bioassay with humans (experiments 3 and 4)

The audio files were tested for their auditory repulsiveness against human volunteers who were informed about our purpose to test their perception of sounds. They also received a short practical introduction on the experimental procedure, that is, about how to launch an audio, to stop walking backward when they felt this as sufficient, and to launch the next audio. Each volunteer was tested individually, by staying in front of a computer placed on a table and coupled to two nearby loudspeakers (Figure 3). The volunteer started the test by pressing the keyboard spacebar, by which a first audio file was played. If the volunteer did not like the sound, the person could walk backward as far as they wished to reach a “comfort distance.” This distance from the loudspeakers was recorded at 0.5 m precision (Figure 3). The person then went back to the computer to launch a second audio file, etc. This setup of experiment 4 was similar to experiment 3 but each audio file was automatically played twice, to give more time to the person in adapting its comfortable distance, which was recorded while the second playing was ending. Each person could give comments after completing the experiment.

Sound pressure (datasets 4 and 5)

All molecule and species audio files used in experiments 3 and 4 were analyzed individually with an application written in Processing (Data S2) to calculate their L_{peak} , in dB.⁶² This is the maximum peak reached by the sound pressure. Other measures, such as average amplitude and root-mean-square amplitude, were also calculated, but L_{peak} turned out to increase the most gradually over the range of analyzed molecules. The gathered dB values for the left ($L_{peakLeft}$) and right ($L_{peakRight}$) channels were then averaged using the formula:

$$L_{peak} = 10 * \log_{10} \left(0.5 * \left(10^{\frac{L_{peakLeft}}{10}} + 10^{\frac{L_{peakRight}}{10}} \right) \right)$$

Alternative mapping conditions

To test the influence of the aforementioned parameter mapping on the correlation between experiment 1 and dataset 4, we measured the L_{peak} from 24 simplified and randomized mapping conditions. The synthesizer used an identical preset, the one previously assigned to aliphatics, now across all 20 molecules. At the level of the mapping, now only three nodes remained constant: the two negatively correlating the number of carbon atoms with the note pitch and equalizer frequency, and the node positively correlating the MW with note duration. Since no esters and ketones occur among the 20 molecules, the mapping of the 4 remaining chemical parameters (i.e., number of acid groups, aldehyde groups, double bonds, and alcohol groups) were randomly attributed, leading to 24 out of 360 possible single-node sets. After recording of the 480 audio files, the L_{peak} values were extracted from them (as explained above, under sonification), and a statistical analysis was performed per set by correlating these values with the results from experiment 1.

Statistical analyses

To compare the variables about single molecules as well as mixtures of molecules, Spearman rank-order correlation tests were applied. These were followed by the false discovery rate control (two-stage sharpened method),^{63,64} which is less conservative than the Holm’s sequential Bonferroni correction. The correlations were computed online using VassarStats.⁶⁵

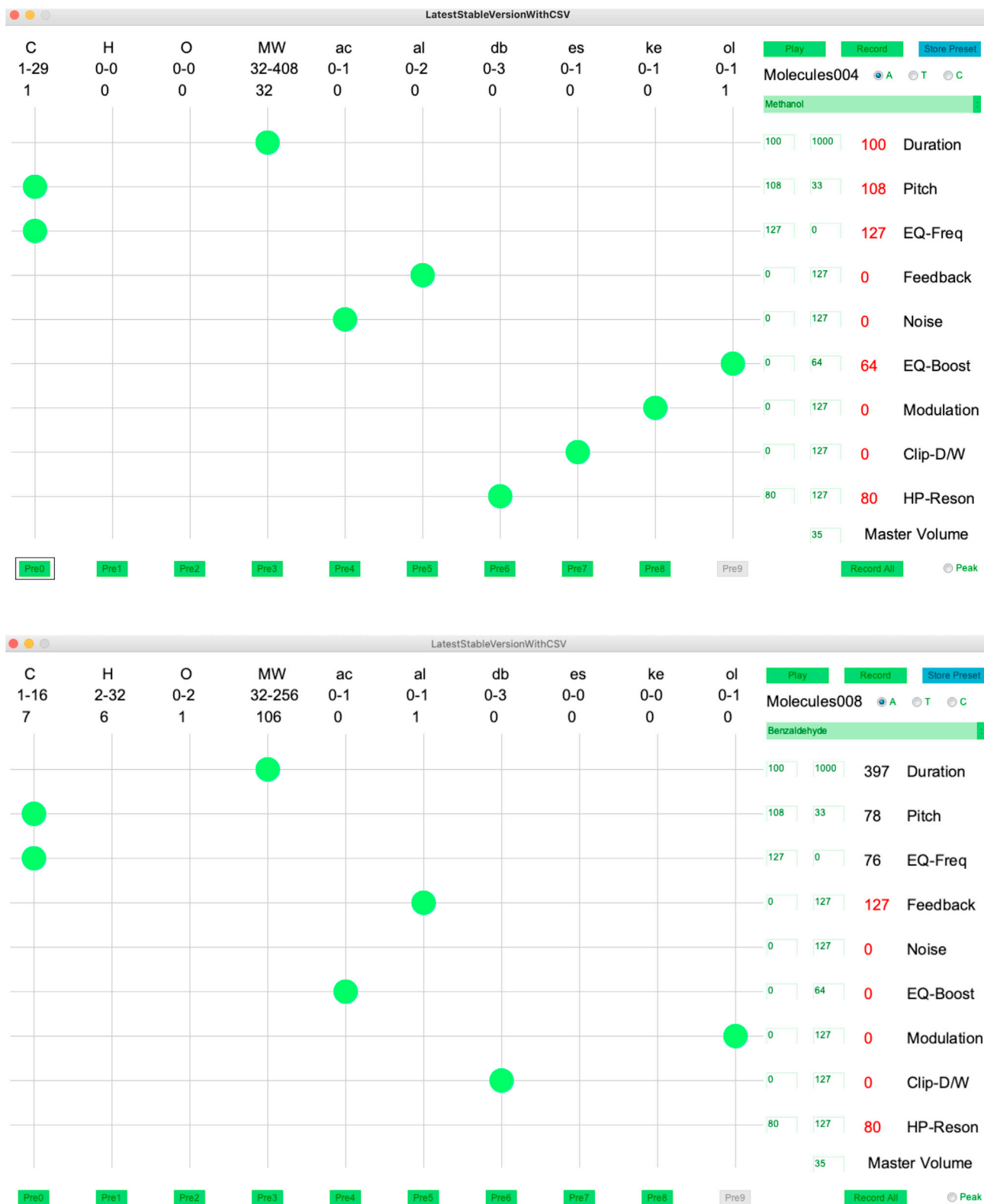


Figure 4. Two illustrations exemplifying the layout interface allowing to set up the parameter mapping via an application

The mapping conditions shown are one used in the main part of the study (above), and the one from alternative mapping conditions (below) that led to the highest significant correlation with the results from experiment 1 (see Table 4, set 17). Practically, at each node a slider allows the activation (green dot) of the linkage between chemical and sound parameters. For details about abbreviations of the chemical parameters (upper row), see Table S1. The second row shows the value

(legend continued on next page)

Ethics approval and consent to participate

This study did not involve endangered or protected insect species. No specific permits were required for this study. Experiments were conducted in accordance with national legislation on the use of animals for research. Experiments 3 and 4 were conducted in accordance with the Declaration of Helsinki. All subjects gave their verbal informed consent for inclusion before they participated in the study, and none of the subjects was under the age of 18 years. These experiments were performed at the Institut de Recherche de l'Institut Supérieur Industriel de Bruxelles, and the experimental protocol was approved by a review board of this institution on February 4, 2019. The review board approved the use of verbal informed consent for these experiments.

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.patter.2021.100352>.

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AUTHOR CONTRIBUTIONS

J.-L.B. elaborated the concept of volatile sonification. J.-L.B. and R.G. designed the sonification process and related experiments. R.G. wrote the codes. J.-L.B. and R.G. gathered the related datasets. J.-L.B. performed bioassays. J.-L.B. analyzed all datasets and wrote main parts of the manuscript. Both authors read and approved the final manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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range as contained in the CSV table (here called "Molecules004" and "Molecules008"; the third row shows the value for the selected molecule. The molecules can be played (Play) and recorded (Record) singly or per batch (Record All), and they can be selected via a drop-down list. For details about the sound parameters (most right-hand column), see text. From right to left, the next column mentions values of duration, in 0.01 s, and MIDI norm for the given molecule; the next two columns mention the extreme MIDI norms used in the linear scaling of chemical parameters for all molecules of the CSV file. See also [Data S2](#).

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