Characterizing honey bee exposure and effects from pesticides for chemical prioritization and life cycle assessment

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ARTICLE INFO

ABSTRACT

Agricultural pesticides are key contributors to pollinator decline worldwide. However, methods for quantifying impacts associated with pollinator exposure to pesticides are currently missing in comparative risk screening, chemical substitution and prioritization, and life cycle impact assessment methods. To address this gap, we developed a method for quantifying pesticide field exposure and ecotoxicity effects of honey bees as most economically important pollinator species worldwide. We defined bee intake and dermal contact fractions representing respectively oral and dermal exposure per unit mass applied, and tested our model on two pesticides applied to oilseed rape. Our results show that exposure varies between types of forager bees, with highest dermal contact fraction of 59 ppm in nectar foragers for lambda-cyhalothrin (insecticide), and highest oral intake fractions of 32 and 190 ppm in nectar foragers for boscalid (fungicide) and lambda-cyhalothrin, respectively. Hive oral exposure is up to 115 times higher than forager oral exposure. Combining exposure with effect estimates yields impacts, which are three orders of magnitude higher for the insecticide. Overall, nectar foragers are the most affected forager type for both pesticides, dominated by oral exposure. Our framework constitutes an important step toward integrating pollinator impacts in chemical substitution and life cycle impact assessment, and should be expanded to cover all relevant pesticide-crop combinations.

1. Introduction

Wild and managed insect pollinators are declining in abundance and diversity worldwide (Potts et al., 2010). Populations of honey bees—among the most important pollinators—have experienced large-scale and rapid losses of adult foragers especially in Europe and the US (Neumann and Carreck, 2010; Van der Zee et al., 2012), with adverse consequences for the entire hives. In specific cases, this phenomenon has been recognized as Colony Collapse Disorder (Watson and Stallins, 2016). Given their important agronomic role, the loss of insect pollinators raises concerns about a potential global crisis for the agrifood sector. The use of biologically active ingredients in plant protection product formulations, hereafter referred to as pesticides, has been identified as one of the main contributors to global pollinator decline (Goulson et al., 2015; Woodcock et al., 2017), along with land-use change, intensive agricultural practice, invasive species, pathogens and climate change (IPBES, 2016). Pesticides can be found in different

components (including nectar and pollen) of wild and cultivated plant species (Fantke and Juraske, 2013; Doucette et al., 2018). Since insect pollinators collect nectar and pollen from a large number of crops, they can be exposed to pesticide residues from contact with pollen or foraging of nectar, depending on the pesticide spray scenario, foraging behavior and shape of the flower, potentially leading to negative effects on the bees. To evaluate and minimize such exposures and related effects when prioritizing or substituting chemicals or when comparing the environmental performance of product and service life cycles, there is an urgent need to consider pesticide-related impacts on bees and other insect pollinators (Fantke et al., 2018a).

Traditionally, environmental impacts are evaluated in the context of ecological risk assessment. Related models for estimating ecotoxicological impacts from exposure of insect pollinators to pesticides have been developed over the years, considering different pathways (Barmaz et al., 2012; Baveco et al., 2016; EFSA, 2013; Poquet et al., 2014; Sanchez-Bayo and Goka, 2016; USEPA, 2014). Higher-tier models allow

for understanding bee population dynamics caused by complex interactions of multiple causes or stressors. For instance, the BEEHAVE model developed by Becher et al. (2014) accounts for multiple stressors (e.g. *Varroa* mites transmitting deformed wing virus, effects of beekeeping practice and food availability, besides pesticide-related effects), either alone or in combination, that affect the development and survival of honey bee colonies. However, approaches that are applicable in risk screening or life cycle based assessments are currently lacking (Crenna et al., 2017). Existing models are mostly receptor-oriented and consider complex interactions between sources and stressors, whereas the boundary conditions of comparative assessment contexts require source-oriented, rapid-screening and fully mass balanced approaches, suitable for application in life cycle impact assessment (LCIA), chemical substitution and alternatives assessment (CAA), and chemical prioritization (Fantke et al., 2018a; Shin et al., 2015; Steingrímsdóttir et al., 2018). Specifically, such boundary conditions include a function-oriented quantitative comparison in terms of potential impacts (e.g. impacts on bees from agricultural pesticides), limited spatiotemporal information about emission data, aiming to reflect representative or typical conditions, aggregation of impacts (e.g. across product life cycles), and quantitatively relating impacts to damage on ecosystem functioning (Fantke et al., 2018a).

In relation to these conditions, existing bee exposure models support agrochemical safety assessments, and generally rely on worst-case assumptions (Christopher Cutler and Scott-Dupree, 2007; Thompson, 2012). Among comparative frameworks, LCIA aims to characterize impact pathways contributing to damages on humans, ecosystems and natural resources associated with product and service life cycles. Ecotoxicity impacts in operational LCIA methods do not differentiate exposure pathways for individual organisms and mostly address impacts on freshwater ecosystems, sometimes used to extrapolate impacts on marine aquatic and soil terrestrial ecosystems, while methods for assessing the various exposure pathways and impacts on insect pollinators (and other aerial organisms) are currently lacking (Crenna et al., 2017; Fantke et al., 2018a).

In a world characterized by a rapidly increasing demand for agricultural-based products (e.g. food, fibers, biofuels), including impacts on insect pollinators associated with exposure to pesticides is furthermore relevant to support decision making (e.g. identifying the best-in-class option among different farming practices, including application technologies and emission reduction strategies), wherever the use of pesticides needs to be considered. In response to this need, the present study aims at proposing a fully mass balance based framework for characterizing ecotoxicity impacts of pesticides on honey bees, chosen as the most economically relevant insect pollinator species worldwide (Rueppell and Kennedy, 2019), for application in life cycle impact and chemical prioritization methods. We focus on three specific objectives: (i) to mathematically describe the overall impact pathway, and define relevant exposure and effect metrics, (ii) to assess oral and dermal exposure for different honey bee worker types, and (iii) to apply the proposed framework in an illustrative case study to characterize honey bee impacts from exposure to two pesticides applied to oilseed rape. With our study, we answer two questions, namely 'Which bee forager type is exposed how much relative to each other?' and 'How does bee forager exposure compare to the total load brought to the bee hive?'

2. Methods

We propose an ecotoxicity characterization framework for honey bees (*Apis mellifera*), developed according to the following steps. We first performed a review of possible exposure pathways of honey bees to pesticides, identifying their predominant exposure pathways. We then defined exposure metrics and developed a characterization framework suitable for being integrated in comparative assessment frameworks. In an illustrative case study, we apply our framework to characterize exposure of honey bees to two example pesticides, and discuss future

research needs to refine and extend our initial framework.

2.1. Review of exposure pathways for insect pollinators

To provide an overview of insect pollinator pathways of exposure to pesticides, we reviewed available guidance documents and scientific literature, focusing on honey bees as an important insect pollinator species. We consulted Web of Science, BioOne, and Google Scholar, searching for terms related to hive composition and foraging behavior (e.g. "pollen/nectar foraging", "foraging trips", "bee forager"), and dynamics of pesticide residues in plants. We retrieved 26 studies, including scientific articles, laboratory- and field-based studies, technical reports from European and international agencies (e.g. EFSA, 2013; USEPA, 2014) and grey literature (e.g. websites of local beekeepers' associations – PRBK, 2018). These studies were used as input to develop our characterization framework and to perform an illustrative case study.

The reviewed studies revealed that depending on the application method (e.g. foliar spray, seed treatment) and on their physicochemical properties, pesticides distribute and can reach different environmental compartments and plant components as residues, to which honey bees can be exposed (Arnold et al., 2012). There are different pathways through which these pollinating insects that forage in-field can be exposed to these pesticide residues (Johnson et al., 2010; Rortais et al., 2005; Sanchez-Bayo and Goka, 2016; Thompson, 2012), whose relevance for causing harm on bees depend on the life stage and forager type of the bees. Honey bee exposure can occur through the following pathways (Fig. 1):

i. Via dermal contact, e.g. when insects fly into the field during pesticide application, through contact with treated plant surfaces (e.g. when collecting pollen and nectar, and to a lesser extent water and guttation drops that can be collected both in-field and off-field) (Kasiotis et al., 2014; Krupke et al., 2012); or through dust dispersed after pesticide seed treatments. Pollen and nectar can directly receive and accumulate pesticide residues (i.e. part of pesticide mass in the environment), while they are at the same time exposure media for bees (Fischer and Moriarty, 2014; Rortais et al., 2005, 2017). Dermal contact to pesticide residues in pollen (via external body contact) and nectar (via internal honey stomach) are possible exposure pathways for forager honey bees (Sgolastra et al., 2019).
ii. Via oral intake (i.e. ingestion) of contaminated pollen, nectar and water, in-field or within the hive, which can be located inside, aside or outside a treated field (Kasiotis et al., 2014; Krupke et al., 2012). Ingestion of residues found in nectar represents one of the most relevant exposure pathways for honey bee foragers (Sanchez-Bayo and Goka, 2016; Sponsler and Johnson, 2017).
iii. Via inhalation of contaminated air, although this pathway is stated to be less relevant for honey bees as compared to dermal contact and oral intake (Sanchez-Bayo and Goka, 2014).

Based on these findings, we focus in our framework on dermal and oral exposure, and further distinguish different bee forager types. Pollen foragers are exposed to pesticide residues in pollen via dermal contact, as they carry pollen balls on specialized hairs on their legs to the hive, and to nectar residues due to ingestion for self-consumption. Nectar foragers are exposed to residues found in nectar, both via dermal contact (they carry nectar into a honey stomach to the hive) and ingestion. As a fraction of nectar foragers may get in contact with pollen, mainly depending on the shape of the flowers, nectar foragers can also be exposed to pesticide residues in pollen via external dermal contact.

2.2. Characterization framework for honey bee exposure to pesticides

To compare the contribution of pesticides to ecotoxicity to honey bees, we calculate for each pesticide a total impact score expressed in
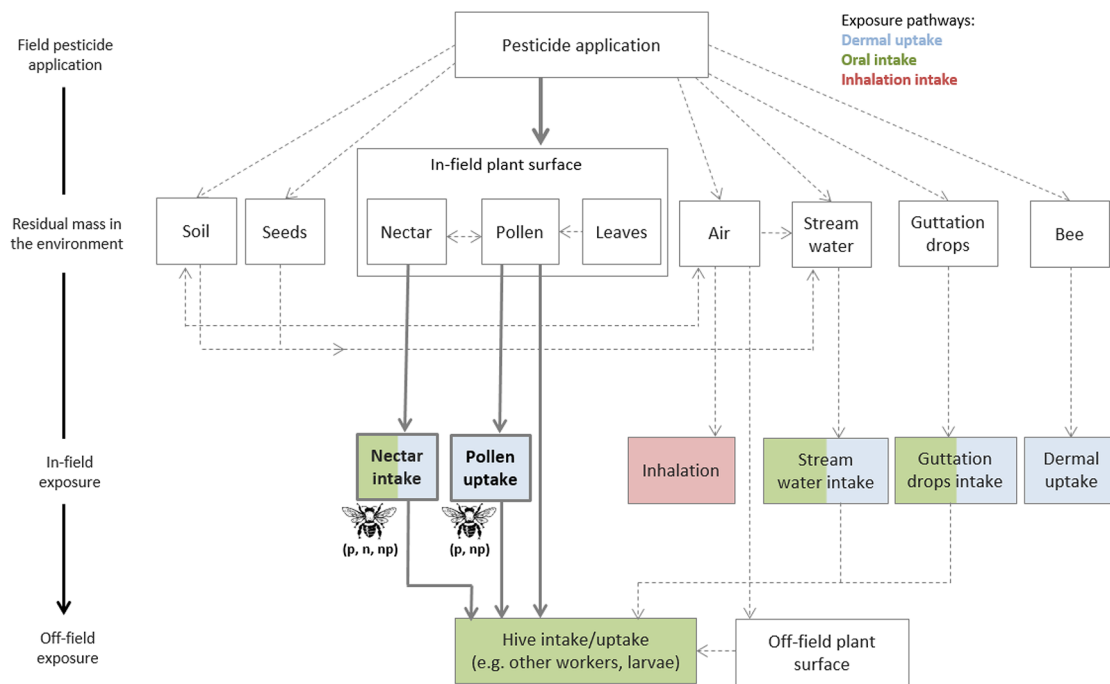
Fig. 1. Conceptual overview of possible exposure pathways of honey bees forager types (p: pollen foragers; n: nectar foragers; np: nectar-pollen foragers) to agricultural pesticides. The main pathways are highlighted as bold lines and are focus in the present study. Other potential pathways and underlying transport processes are represented as dashed lines.

number of bees affected per hectare of treated crop, IS_{total} [bees$_{affected}$/ha], given by the sum of $IS_{forager i}$ and IS_{hive}, that quantifies the number of bees affected per treated area, as:

$$IS_{total} = \sum_{forager\ i} \underbrace{(m_{appl} \times [CF^{oral}_{forager\ i} + CF^{dermal}_{forager\ i}])}_{IS_{forager\ i}} + \underbrace{m_{appl} \times CF^{oral}_{hive}}_{IS_{hive}}$$

$$= m_{appl} \times CF_{total} \tag{1}$$

where $CF^{x}_{forager i}$ [bees$_{affected}$/kg$_{applied}$] represent forager characterization factors, which depend on forager type i and exposure route x (i.e., oral or dermal exposure), CF^{oral}_{hive} [bees$_{affected}$/kg$_{applied}$] represent hive characterization factors related to oral intake of pesticides by all bees inside the hive and m_{appl} [kg$_{applied}$/ha] is the mass of pesticide applied. We then derive the potentially affected fractions of bees, $PAF_{forager i}$ and PAF_{hive} [bees$_{affected}$/ha per bees/ha], for each specific type of honey bees by dividing the total impact score for each pesticide by the related density of honey bees, N [bees/ha], as:

$$PAF_{forager\ i} = IS_{forager\ i}/N_{forager\ i} \tag{2a}$$

$$PAF_{hive} = IS_{hive}/N_{hive} \tag{2b}$$

The density of bees per hectare is derived from the number of bees per hive and the crop-specific number of hives per hectare (see Supplementary Information, Section S-3.1).

To characterize ecotoxicological impacts of pesticides on bees, we define characterization factors, CFs [bees$_{affected}$/kg$_{applied}$], which quantify the number of affected bees per unit mass of pesticide applied in the agricultural environment, thus allowing the comparison across a broad variety of pesticides. Characterization factors are calculated separately for both oral and dermal exposure to reflect potential differences in exposure route-specific effects. Adapting the concept of intake fraction commonly used to characterize human exposure to chemicals (Bennett et al., 2002; Fantke et al., 2018b), and expanding this concept by introducing dermal contract fractions, we calculate characterization factors for each affected bee type as the product of exposure and effect metrics:

$$CF^{oral}_{forager i} = iF_{forager i} \times EF^{oral} \tag{3a}$$

$$CF^{dermal}_{forager i} = sF_{forager i} \times EF^{dermal} \tag{3b}$$

$$CF^{oral}_{hive} = iF_{hive} \times EF^{oral} \tag{3c}$$

where the *bee oral intake fraction*, $iF_{forager i}$ [kg$_{oral-intake}$/kg$_{applied}$], and *bee dermal contact fraction* with skin or honey stomach, $sF_{forager i}$ [kg$_{dermal-contact}$/kg$_{applied}$], include both environmental fate and exposure processes and characterize the mass of pesticide taken up via respectively oral or dermal exposure by bee type (different forager types i and in-hive bees) per unit mass of pesticide applied; and where EF^{oral} [bees$_{affected}$/kg$_{oral-intake}$] and EF^{dermal} [bees$_{affected}$/kg$_{dermal-contact}$] are the effect factors relating the number of bees affected to respectively oral and dermal exposure. EFs are based on generic effect data for honey bees due to missing data for different bee types (e.g. foragers). CFs for oral and dermal exposure can be summed up to give an overall CF for the selected pesticide, characterizing the in-field impact on bees per unit mass of applied pesticide. This assumes equal weighting for effects on different bee types due to currently missing information on the relevance of forager type or other bees for the overall hive. Individual CFs account for the specific exposure route, the characteristics of the foragers (e.g. their tasks, their behavior in field), the physicochemical properties of the pesticides, the environmental conditions and the crop species. We also calculated CFs for in-hive exposure, in terms of bees affected using the same oral effect factor as for the foragers, due to lack of data on specific effects for larvae, other bees and queen. The amount of pesticide brought into the hive via pollen and nectar by the foragers is determined by mass balance, and is assumed to be entirely ingested by the bees inside the hive.

In line with current LCIA recommendations (EC-JRC, 2011), we aim at parameterizing the influential factors contributing to bee exposure variability, such as seasonal fluctuations and the change in the foraging sources, that may push the colony to adjust the ratios of individual bees engaged in the different tasks (Robinson, 1992). We thus consider a fixed number of honey bees, acting as individuals (individual-based modeling), foraging in a crop field rich in food sources (i.e. during the crop flowering period). The crop field does not have a specific spatial extent or shape (Rosenbaum et al., 2015). We assume that honey bees

follow a simple set of rules, namely: (i) foragers fly out of the hive towards a patch of flowers, (ii) collect pollen or nectar or both at the flowers in the crop field, (iii) fly back to the hive, (iv) unload the food at the hive, and then (v) set out again on their next trip. The hives are assumed to be located at the edge of the field; considering that, when food is sufficiently abundant in the vicinity of the hives, honey bees forage within a radius of approximately 1 km (Seeley, 1995; Villa et al., 2000).

Division of labor in honey bee colonies is characterized by tasks performed by specialized individuals. Hence, our characterization framework is developed for pollen foragers and nectar foragers, of which the latter include individuals that uniquely go for nectar and individuals that additionally may get in touch with pollen (Bohart and Nye, 1956). We considered pollen and nectar as different pesticide residue compartments used as forager source. We quantify exposure of pollen and nectar foragers separately due to their different behavior in the field and inside the hive. Further details on these behaviors are found in the Supplementary Information (Section S-2). We retrieved information on the most relevant parameters characterizing honey bee in-field behavior (e.g. foraging activity, flying period and time) from the ecological literature and on pesticides application (e.g. application type, time and frequency) from pesticide labels and risk assessment reports.

2.2.1. Forager oral exposure

Oral exposure occurs when a honey bee gets in contact with contaminated nectar via ingestion. Both pollen foragers and nectar foragers feed themselves with nectar, to get the necessary energy to fly. Therefore, the forager oral intake fraction $iF_{forageri}$ [$kg_{oral\text{-}intake}/kg_{applied}$] is calculated for both forager types:

$$iF_{forageri} = \frac{N_{forageri} \times Q^{oral}_{forageri,nectar} \times \int_{t_0}^{t_1} C_{nectar,x,y} dt}{m_{appl,x,y}} \tag{4}$$

where $N_{forageri}$ [bees/ha] is the density of the specific type of honey bee foragers on field, for $i \in \{p, n, np\}$, with index p, n and np respectively referring to pollen foragers, nectar foragers and nectar foragers that also get in contact with pollen; $Q^{oral}_{forageri,nectar}$ [kg/bee/d] for $i \in \{p, n, np\}$ is the daily individual nectar consumption rate; $\int_{t_0}^{t_1} C_{nectar,x,y} dt$ [kg/d/kg_{nectar}] is the residual concentration of pesticide x in nectar of crop species y within the flowering period, integrated over the entire exposure and flowering period, t_0 being either the start of the flowering period or the time of application if the flowering period has already started, and t_1 the end of the flowering period; and $m_{appl,x,y}$ [$kg_{applied}$/ha] is the application rate of pesticide x to crop y.

$N_{forageri}$ depends on the colony's characteristics (i.e. size and structure), which in turn rely on several external and internal factors, such as the availability of food and, in case of managed colonies, on beekeeping practice (Becher et al., 2014). Honey bee colonies are dynamic, which means that the worker population can vary in size and structure over time depending on the season and on the needs of the hive. We consider an average fixed fraction for each type of honey bee foragers, according to the available literature (Supplementary Information, Table S2).

$Q^{oral}_{forageri,nectar}$ is forager type-specific. We used the average consumption rate according to the USEPA Guidance for Assessing Pesticide Risks to Bees (USEPA, 2014), which provides specific information on the amount of nectar consumed by each type of honey bee forager (Supplementary Information, Table S6).

Finally, the time-integrated residual concentration of pesticide in nectar is calculated as:

$$\int_{t_0}^{t_1} C_{j,x,y} dt = \frac{C_{j,x,y}(t_0)}{k_{j,x,y}} \times [e^{-k_{j,x,y} \times t_0} - e^{-k_{j,x,y} \times t_1}] \tag{5}$$

where $C_{j,x,y}(t_0)$ [kg/kg_{nectar}] is the initial concentration of pesticide x in j = nectar of crop y, coming from measured data; and $k_{j,x,y}$ [d^{-1}] represents the first-order rate constant for dissipation, by both

degradation and dilution, of the pesticide in j = nectar. The ratio of the time-integrated residual concentration over the initial concentration then yields the average attenuation factor as $C_{j,x,y}(t)/C_{j,x,y}(t_0) = (e^{-k_{j,x,y} \times t_0} - e^{-k_{j,x,y} \times t_1})/(k_{j,x,y} \times [t_1 - t_0])$.

2.2.2. Forager dermal exposure

Dermal exposure occurs when a honey bee gets in contact with contaminated pollen or nectar via body contact after a given exposure duration. Contact may occur externally (i.e. at skin level, via pollen contact with a fraction of honey bee body) or internally (i.e. at honey stomach level, via nectar contact). The dermal contact fraction $sF_{forageri}$ [$kg_{dermal\text{-}contact}/kg_{applied}$] represents the fraction of the applied pesticides that is in dermal contact with the bee via its skin or honey stomach, calculated for both pollen and nectar foragers as:

$$sF_{forageri} = \frac{N_{forageri} \times Q^{dermal}_{forageri,j} \times fr_A \times \int_{t_0}^{t_1} C_{j,x,y} dt}{m_{appl,x,y}} \tag{6}$$

where $N_{forageri}$ [bees/ha] is the density of the specific type of honey bee foragers on field, for $i \in \{p, n, np\}$; $Q^{dermal}_{forageri,j}$ [kg/bee/d] is the quantity of $j \in \{pollen, nectar\}$ per day that is in dermal contact with the skin or honey sack of bees $i \in \{p, n, np\}$; fr_A [$-$] is the fraction of honey bee foragers' body surface area exposed to pesticide residues in j = pollen; $\int_{t_0}^{t_1} C_{j,x,y} dt$ [kg/d/kg_j] for $j \in \{pollen, nectar\}$ is the time-integrated residual concentration of pesticide x in nectar/pollen of crop species y within the flowering period, integrated over the entire exposure and flowering period; and $m_{appl,x,y}$ [$kg_{applied}$/ha] is the applied mass of pesticide x to crop y.

$Q^{dermal}_{forageri,j}$ is itself calculated as a function of two parameters as $Q^{dermal}_{forageri,j} = M_{forageri,j} \times fr_{forageri}$, where $M_{forageri,j}$ [kg_j/bee/d] is the daily load carried by each specific type of honey bee forager, for $i \in \{p, n, np\}$ and $j \in \{pollen, nectar\}$; and $fr_{forageri}$ [d/d] represents the daily exposure time fraction for $i \in \{p, n, np\}$, namely the fraction of time over a day during which a forager honey bee is exposed to pesticide residues.

$M_{forageri,j}$ varies according to honey bee forager type and the specific foraging behavior (Supplementary Information, Table S3). Specifically, $M_{forageri,j}$ for j = pollen corresponds to an average full pollen load for pollen foragers (i = p), while nectar foragers which get in contact with pollen (i = np) generally return to the hive before the pollen baskets are full (Bohart and Nye, 1956). Therefore, for the former we set this parameter at the average amount of pollen daily carried by individual honey bees, while for the latter we set the value at the minimum amount of pollen load found in the literature. The value of $M_{forageri,j}$ for j = nectar is fixed at the average daily nectar load for all nectar foragers. Detailed values of these daily loads are reported in the Supplementary Information (Table S3). The exposure time fraction $fr_{forageri}$ [d/d] is derived as the fraction of time over a day that an individual honey bee spends collecting, actively or not, pollen and nectar in the crop field, flying back into the nest and unloading:

$$fr_{forager\ i} = fr^{foraging}_{forager\ i} + fr^{flying\ in}_{forager\ i} + fr^{unloading}_{forager\ i} \tag{7}$$

The foraging behavior is derived from the field of ecology, and the exposure time fraction depends on the honey bee forager type (Fig. 2). Detailed information and the specific values used in calculations are reported in the Supplementary Information (Tables S4 and S5).

The body surface area of forager honey bees exposed to pesticide residues in pollen is derived as the ratio between the mean apparent exposure surface area and the mean total physical surface area, as defined in Poquet et al. (2014). The time-integrated residual concentration of pesticides in pollen is calculated as above for nectar (Eq. (5)), based on empirically measured data of pesticide residues in pollen and the dissipation rate of the pesticide in pollen.

2.2.3. Hive oral exposure

In addition to the forager exposure, the pesticide transported via the pollen and nectar to the hive is assumed to be ingested orally by all bees
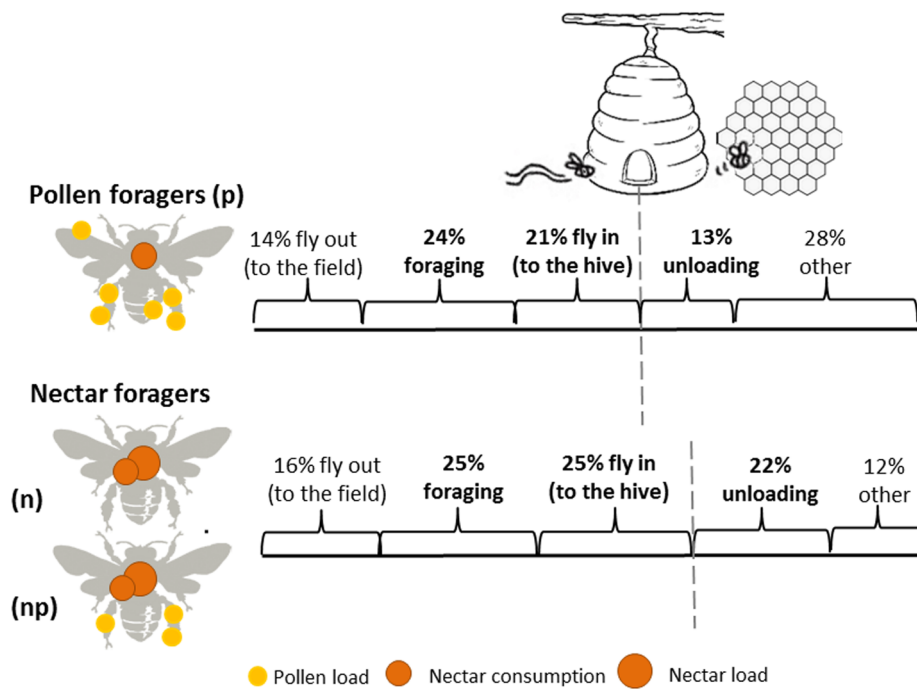
Fig. 2. Exposure time fractions for different honey bee forager types during a foraging trip, based on their type-specific behavior in-field.

in the hive. The hive intake fraction can be derived from the load of pollen and nectar brought to the hive, $M_{\text{forager}i,j}$ [kg_j/bee/d], as:

$$iF_{\text{hive}} = \frac{\sum_{\text{forager } i \in \{n,np\}} N_{\text{forager } i} \times M_{\text{forager } i,\text{nectar}} \times \int_{t_0}^{t_1} C_{\text{nectar},x,y} dt}{m_{\text{appl},x,y}}$$

$$+ \frac{\sum_{\text{forager } i \in \{p,np\}} N_{\text{forager } i} \times M_{\text{forager } i,\text{pollen}} \times \int_{t_0}^{t_1} C_{\text{pollen},x,y} dt}{m_{\text{appl},x,y}} \tag{8}$$

where $M_{\text{forager}i,j}$ [kg_j/bee/d] is the daily load carried by each specific type of honey bee forager, for $i \in \{p, n, np\}$ and $j \in \{pollen, nectar\}$.

2.2.4. Ecotoxicity effects

The effect factor (EF) [$bees_{\text{affected}}$/$kg_{\text{intake or dermal-contact}}$] relates the oral and dermal exposure to an equivalent number of affected honey bees. This factor depends on the ecotoxicity potency that the pesticide exerts on bees and is derived as:

$$EF^x = \alpha/LD50^x \tag{9}$$

where $LD50^x$ [kg/bee] for $x \in \{oral, dermal\}$ is the amount of pesticide taken in or up by an exposed honey bee population, that affects 50% of the exposed bee population over background with death as specified effect endpoint, and $\alpha = 0.5$ refers to the response level of 50% corresponding to these LD50 data. LD50 data are generally available from acute oral and contact toxicity tests, conducted on adult worker honey bees. However, in LCIA a long-term perspective is considered; hence lifetime exposure and related chronic effects in bees are needed. To our knowledge, data from chronic oral and contact toxicity tests on adult forager honey bees are not widely available. Therefore, we prioritize chronic LD50 data and use acute LD50 as proxy where chronic data are missing, being aware that further research is required to account for chronic effects. We use LD50 of adult bees as proxy for both larvae and other hive bees, to preliminarily explore the effects of pesticides in the hive.

2.3. Case study definition

We applied the proposed characterization framework in an illustrative case study to two pesticides applied to oilseed rape (*Brassica napus*) as example crop. Honey bees are the main pollinators of oilseed rape, one of the most cultivated crops in Europe, and can account for up

to 95% of all insect pollinators of this crop (Viik, 2012). Since honey bees that forage on oilseed rape can collect nectar either getting in contact with pollen or not (Westcott and Nelson, 2001), we considered all forager bee types $i \in \{p,n,np\}$ in our case study. Our case study scenarios represent central/northern European conditions, for example with respect to number of bees per hive.

We retrieved information on the possible pests occurring on oilseed rape in Europe during its flowering period (Williams, 2010), which corresponds to the honey bees' active foraging season. We then determined pesticides applied against these pests with focus on pesticides applied as foliar spray. We identified two pesticides, namely boscalid (CAS 188425-85-6, carboxamide fungicide) and lambda-cyhalothrin (CAS 91465-08-6, systemic pyrethroid insecticide). Both pesticides are authorized in the European Union and registered by various Member States for application to blooming oilseed rape plants, with restrictions for lambda-cyhalothrin, not being allowed for use during the active flying hours of honey bees (EFSA, 2014). Boscalid, which inhibits spore germination (PPDB, 2019), does not primarily target insects with its mode of action. Lambda-cyhalothrin, in contrast, disrupts the functioning of the nervous systems in living organisms and is used to control aphid, coleopterous, and lepidopterous pests.

For these two pesticides, we collected application data. The flowering period of oilseed rape may differ between countries according to climate conditions. Therefore, we estimated an average flowering scenario of 24 days for oilseed rape in Europe (Supplementary Information, Table S7) from the AppDate software (Klein, 2012). AppDate was developed for calculating reasonable application dates for different crops at selected locations in Europe based on crop life-cycle stages. We defined our bee exposure scenario by assuming a single application at the beginning of the flowering period (t_0), and determined the length of the exposure period for calculating the time-integrated residual concentration in pollen and nectar (Supplementary Information, Table S8; additional analysis on residues in Tables S9 and S10). According to Good Agricultural Practice (GAP) (FAO, 2016), a second application is not always necessary and it generally falls outside the flowering period. Finally, we collected toxicity data (either reflecting oral or dermal exposure) of both pesticides to honey bees (Supplementary Information, Table S11). In cases where toxicity tests

reported "higher-than" value, we selected the reported numeric value based on a conservative assumption.

In our case study, we test our proposed framework along illustrative scenarios, which reflect possible but not necessarily most representative practices. When applying our framework in actual substitution, prioritization or life cycle impact studies, the respective most representative scenarios should be defined, which might also include recommended scenarios from product labels.

As input data for our model vary within specific ranges (Supplementary Information, Section S-3), we conduct a Monte Carlo uncertainty analysis, where we randomly varied all model inputs in 100,000 realizations according to uniform distributions of parameters within their range of variation. The outputs are reported in the Supplementary Information (Section S-5).

3. Results

3.1. Bee oral intake and dermal contact fractions

Pesticide mass applied, initial concentration in pollen and nectar, and dissipation rate as well as density of forager bees and their behavior in-field and in the hive are the main aspects that determine pesticide-specific oral intake and dermal contact fractions for bees. Table 1 presents the average values for these aspects collected from literature data. Initial pesticide concentrations are 2 to 10 times higher in pollen than in nectar, and are higher for boscalid than for lambda-cyhalothrin, reflecting the high mass of boscalid applied. However, initial concentrations per unit mass applied are higher for lambda-cyhalothrin, with concentration per kg applied as compared to boscalid being 3.8 and 18.5 times higher respectively in pollen and in nectar. Differences in subsequent bee exposure between these chemicals will be primarily driven by pesticide dissipation, which is 3 to 5 times faster for lambda-cyhalothrin than for boscalid. This results in a stronger attenuation during the flowering period for lambda-cyhalothrin, with an average concentration equal to 3% of the initial concentration as compared to 9% to 16% for boscalid (Table 1a). However, this is not enough to compensate the higher initial concentration per unit mass applied for lambda-cyhalothrin. For the quantities of nectar ingested and in dermal contact, the highest exposure is observed for nectar ingestion by nectar foragers (Table 1b and Supplementary Information, Section S-3). For pollen, despite lower load per trip for the nectar-pollen forager, their pollen load is higher than for the pollen forager due to more than 3 times longer exposure duration for the nectar foragers.

Both oral intake and dermal contact fractions vary with the specific type of forager bees (Supplementary Information, Table S12). Nectar foragers generally show highest exposure fractions, dominated by oral intake and ranging from 32 ppm for boscalid to 190 ppm for lambda-cyhalothrin, reflecting the larger number of nectar foragers in the hive and the high daily intake of nectar per nectar forager bee. Dermal exposure across forager types is generally lower than oral exposure, with highest dermal contact fractions falling in the range of 15 to 59 ppm for lambda-cyhalothrin. Dermal contact fractions are lower for boscalid. For both pesticides, nectar forager bees get the highest exposures per bee via dermal contact, due to their long exposure duration (Table 1). Oral exposure per bee is also higher for the nectar and nectar-pollen foragers, since nectar intake dominates overall exposure.

For comparison, we evaluated exposure separately for foragers (direct contact with pollen and nectar at the flowers) and for in-hive bees (contact with nectar and pollen that was not consumed by the delivering foragers). Based on this comparison, cumulative in-hive oral exposure is higher than forager exposure for both pesticides. For boscalid, it is up to 115 times higher, and for lambda-cyhalothrin, it is up to 32 times higher than oral exposure of foragers. This is partly related to the high number of bees exposed inside the hive (42,055 in-hive bees as compared to 13,445 forager bees). Variability of hive oral exposure depends on the range of values for pollen and nectar loads, as the mass-balance based bee oral intake fraction, iF_{hive}, is derived from the amount of pollen and nectar brought to the hive by foragers (see Eq. (8)).

Fig. 3 shows the results of the Monte Carlo uncertainty analysis, in which we compare the oral and dermal exposure to boscalid and lambda-cyhalothrin residues in oilseed rape pollen and nectar for all

Table 1

Main aspects determining pesticide oral intake and dermal contact fractions of bees: (a) physicochemical properties and initial concentrations of case study pesticides in pollen and nectar, and (b) bee characteristics.

(a) Pesticide characteristics	Boscalid	Lambda-cyhalothrin
Mass of pesticide applied per unit area [$kg_{applied}$/ha]	0.250[a]	0.0075[b]
$C_{pollen}(t_0)$: initial pesticide concentration in pollen [kg/kg_{pollen}]	1.39×10^{-5a}	1.59×10^{-6b}
$C_{nectar}(t_0)$: initial pesticide concentration in nectar [kg/kg_{nectar}]	1.43×10^{-6a}	7.93×10^{-7b}
k_{pollen}: pesticide dissipation rate in pollen [d^{-1}]	0.25[c]	1.33[d]
k_{nectar}: pesticide dissipation rate in nectar [d^{-1}]	0.43[c]	1.33[d]
Average attenuation factor[e] in pollen during flowering period [–]	0.16	0.031
Average attenuation factor[e] in nectar during flowering period [–]	0.096	0.031
log K_{ow} [–]	2.96[f]	6.80[f]
Henry's law constant at 25 °C [Pa m³/mol]	5.18×10^{-5} [g]	2.00×10^{-2} [g]

(b) Bee characteristics	Pollen forager	Nectar forager	Nectar-pollen forager
Density of forager bees [bees/ha]	3538	8208	1698
$M_{forager\ i,nectar}$: nectar load per day and per bee [kg/bee/d]	–	3.25×10^{-4}	3.25×10^{-4}
$M_{forager i,pollen}$: pollen load per day and per bee [kg/bee/d]	2.00×10^{-4}	–	1.00×10^{-4}
$Q_{forager i,nectar}^{oral}$: quantity of nectar ingested per day and per bee [kg/bee/d]	4.35×10^{-5}	2.92×10^{-4}	2.92×10^{-4}
$Q_{forager i,nectar}^{dermal}$: quantity of nectar in dermal contact per day and per bee [kg/bee/d]	–	9.05×10^{-5}	9.05×10^{-5}
$Q_{forager i,pollen}^{dermal}$: quantity of pollen in dermal contact per day and per bee [kg/bee/d]	1.63×10^{-5}	–	2.78×10^{-5}

[a] 50 g a.i./100 g product × 500 g product/ha = 250 g a.i./ha = 0.250 kg/ha (Wallner, 2009).
[b] 100 g a.i./L product × 0.075 L product /ha = 7.5 g/ha = 0.0075 kg/ha (Choudhary and Karma, 2008; Syngenta, 2018).
[c] Based on half-life in pollen and nectar reported in Wallner, 2009.
[d] Based on half-life in pollen and nectar reported in Choudhary and Karma, 2008.
[e] see explanation below Eq. (5).
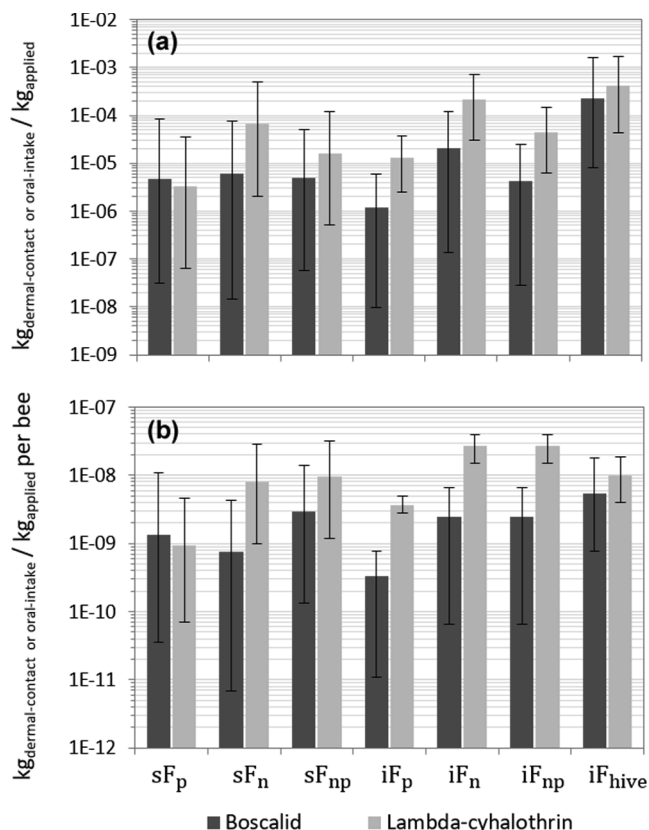[f] Kim et al., 2015.
[g] EFSA, 2018.

Fig. 3. Comparison between dermal contact (sF) and oral intake (iF) fractions of different honey bee forager types, with error bars indicating minimum to maximum variability from the Monte Carlo analysis: pollen foragers (p), nectar foragers (n), and nectar foragers additionally in contact with pollen (np), for the fungicide boscalid and the insecticide lambda-cyhalothrin, expressed as total exposure fractions (a) and as exposure fractions per bee (b), both in logarithmic scale.

populations of forager types and in-hive bees. Columns represent averages across 100,000 realizations. The outcomes of the Monte Carlo analysis overlap with the results of our model (Supplementary Information, Section S-5).

3.2. Case study effect and characterization results

Effect factors depend on the ecotoxicity potential of pesticides on honey bees and are presented in Table 2. The insecticide lambda-cyhalothrin shows 800 to 5,000 times higher effect factors for both oral and dermal exposure than the fungicide boscalid, based on its higher tested acute ecotoxicity compared to the chronic ecotoxicity of boscalid. The LD50 for dermal exposure is much lower than for oral exposure, indicating highest effect potency of lambda-cyhalothrin via dermal contact.

Multiplying the effect factors by the exposure fractions yields the ecotoxicity impact characterization factors, CFs, for each bee type (Eq. (3)). Fig. 4a presents the effect factors as a function of exposure fractions, the diagonal iso-lines representing equal CFs. The further up a point is over the diagonal, the higher the impact per kg applied. For boscalid, the impact per kg applied is dominated by oral exposure of in-hive bees with 1,181 bees affected per kg applied (black filled diamond), about 1.5 orders of magnitude higher than oral and dermal exposure of nectar foragers (black filled and empty triangles, respectively) and between two and three orders of magnitude higher than dermal exposure of the other forager types (empty square and circle). The resulting total impact per kg of lambda-cyhalothrin applied is at least two orders of magnitude higher due to the combination of

substantially three to four orders of magnitude higher exposure and effect factor. In-hive oral exposure remains among the highest exposure pathways (grey filled diamond), but the impact per kg applied is even higher for dermal contact of nectar foragers (close to 10^6 bees affected per kg applied), due to the even higher dermal effect factor. In the absence of information on the respective relevance of forager types for the whole hive, we considered equal weighting across bees and summed up all related CFs to a single overall pesticide-specific CF (second last row in Table 2). The overall CF of boscalid is at about three orders of magnitude lower than the overall CF of lambda-cyhalothrin, with boscalid and lambda-cyhalothrin potentially affecting 1,260 and 1,360,000 bees per kg applied, respectively.

Multiplying the overall CFs by the mass applied per ha finally yields the total impact score per ha for each pesticide, IS (last row in Table 2). The values obtained are represented in Fig. 4b, the diagonal iso-lines corresponding to equal IS. It shows that the 33 times higher mass applied per hectare of boscalid is not sufficient to compensate for the three orders of magnitude higher CFs for lambda-cyhalothrin. The resulting IS of lambda-cyhalothrin, with 10,172 of all bees affected, is more than thirty times higher than the IS of boscalid with 314 out of 55,500 bees affected.

Fig. 5 details the potentially affected fraction for each type of bees (PAF, y-axis), combined with the corresponding fraction of each bee type per ha (x-axis), with bee types ranked from highest to lowest PAF. The overall area of this graph corresponds to the total impact score (IS$_{total}$) per pesticide. It demonstrates that the application of lambda-cyhalothrin leads to very high PAFs for the nectar foragers (n, np), up to 94%, due to the high potential dermal toxicity and exposure to this substance. For boscalid, the potentially affected fraction of bees is restricted, below 1% for all bee types, and the large number of in-hive bees makes the oral exposure of in-hive bees the dominant contributor to the overall impact score for this pesticide.

Overall, the exposure of honey bee foragers to pesticide residues in nectar, both via oral and dermal exposure, represents the most noticeable issue for both pesticides, of which the insecticide lambda-cyhalothrin shows highest impacts on honey bee forager populations compared to the fungicide boscalid.

4. Discussion

4.1. Applicability of the characterization framework

Characterization results developed in this study synthesize exposure and ecotoxicity effect information for honey bees into cumulative values and are applicable in comparative assessments, including chemical substitution and prioritization, and LCIA.

More complex, higher-tier risk assessment models like BEEHAVE (Becher et al., 2014) are able to account for interactions between different stressors and focus on the receptors (i.e. bee population dynamics). In contrast to this, our proposed approach does not aim at predicting honey bees survival, but provides a relative indicator across a potentially large number of pesticides applied at different rates on different crops. At this level, causes of impacts are evaluated separately in line with current LCIA and substitution frameworks. In fact, our factors allow to compare specific sources for a particular cause (in this case pesticides) as part of a comparative evaluation of various impacts (climate change, human toxicity, ecotoxicity, land use, etc.) of entire production systems, or to rapidly compare the potential impacts of hundreds of pesticides across multiple crop production systems.

Our factors are based on a consistent chemical mass balance and use best estimates, which meet the boundary conditions of quantitative and comparative frameworks.

The application of our characterization framework in the illustrative case study enabled a comparison between two different pesticides, helping identify in a given scenario the pesticides with the highest impact potential for bees that collect either pollen or nectar.

Table 2

Ecotoxicity test data for honey bees, respective estimated effect factors associated with both dermal and oral exposure, and calculated characterization factors and impact scores for two case study pesticides.

Factor	Boscalid	Lambda-cyhalothrin
Acute LD50 contact for adult bees [µg/bee]	200[a,b]	0.038[b,c]
Acute LD50 oral for adult bees, also as proxy for hive bees [µg/bee]	–	0.91[b,c]
Chronic LD50 oral for adult bees [µg/bee]	760[d]	–
Chronic LD50 oral for larvae, as proxy for hive bees [µg/bee]	75.19[e]	–
EF dermal for all foragers [bees$_{affeted}$/kg$_{dermal\ contact}$]	2.50×10^6	1.32×10^{10}
EF oral for all foragers [bees$_{affected}$/kg$_{oral\ intake}$]	6.58×10^5	5.49×10^8
EF oral for hive bees [bees$_{affected}$/kg$_{oral\ intake}$]	5.00×10^6	5.49×10^8
CF for pollen foragers [bees$_{affected}$/kg$_{applied}$]	11.5	4.55×10^4
CF for nectar foragers [bees$_{affected}$/kg$_{applied}$]	46	8.80×10^5
CF for nectar-pollen foragers [bees$_{affected}$/kg$_{applied}$]	17.8	2.14×10^5
CF for hive bees [bees$_{affected}$/kg$_{applied}$]	1.18×10^3	2.17×10^5
CF total across all bees [bees$_{affected}$/kg$_{applied}$]	1.26×10^3	1.36×10^6
IS total across all bees [bees$_{affected}$/ha]	3.14×10^2	1.02×10^4

[a] EFSA, 2018.
[b] PPDB, 2018.
[c] EFSA, 2014.
[d] Simon-Delso et al., 2018.
[e] Simon-Delso et al., 2017.

Lambda-cyhalothrin as one of the pesticide evaluated in our case study has a high octanol-water partition coefficient (K_{ow}), meaning that it tends to partition into lipids (see Table 1). The lipophilic nature of lambda-cyhalothrin makes it readily absorbable by biological tissues, such as the insect skin, disrupting nerve conduction and leading to eventual death (He et al., 2008). Boscalid has a lower K_{ow} than lambda-cyhalothrin, suggesting that it is less lipophilic. However, its persistence and intense application to certain crops may lead to long periods of exposure for honey bees (Simon-Delso et al., 2018). This difference between the two case study pesticides is well-reflected by our impact characterization factors, which are two to four orders of magnitude higher for lambda-cyhalothrin on a per kg applied basis (including impacts related to in-hive exposure), but also on a per ha treated area basis, supporting that this insecticide is not allowed for use during the active flying hours of honey bees (EFSA, 2014).

In order to apply our exposure and ecotoxicity characterization factors, which are linked to mass applied, in an LCIA context, pesticide application data need to be included in emission inventories, since emission data are often not available to practitioners (Fantke and Jolliet, 2016; Rosenbaum et al., 2015).

When addressing exposure and impacts on bees, it is moreover important to collect and keep additional information, such as pesticide application rates and application times in relation to active bee foraging periods.

4.2. Limitations in exposure and effect estimates

Our proposed characterization framework has several limitations, mostly related to input data, considered exposure pathways, and effect assessment. The framework builds on a single set of measured pesticide residual concentrations in pollen or nectar due to the poor availability of similar information. Generally, data on residues in pollen and nectar from a single crop species are limited to few studies due to the fact that (i) for economic purposes and to protect consumer health, honey (or food, in general) is itself well-studied, while pollen and nectar as source matrices are less studied; and (ii) residues are generally measured as multi-residues, without differentiating among original crop species. Additionally, measured residue content in these matrices may present high variability, depending on pesticide application rate and technique, selected crop species, season, location, etc. (Gierer et al., 2019), which may all influence pesticide persistence and distribution in the plant-environment system (Bonmatin et al., 2015). We also compared
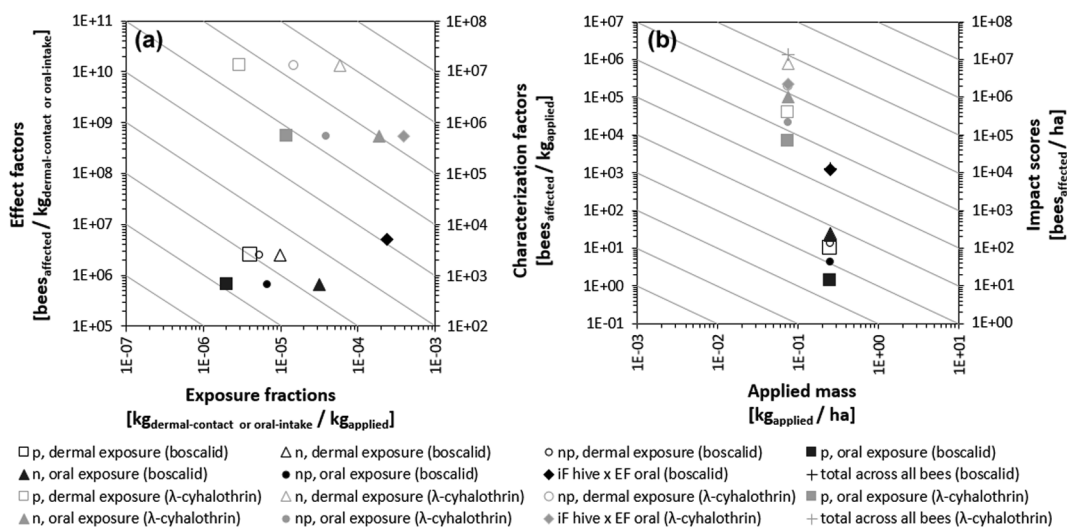

Fig. 4. Contribution of the oral (filled) and dermal (empty symbols) exposure for each bee forager type and in-hive bees, to (a) characterization factors (impact per kg applied) and (b) impact score (impact per ha) for boscalid (black) and lambda-cyhalothrin (grey), with p = pollen foragers (□); n = nectar foragers (o); np = nectar foragers in contact with pollen (Δ); in-hive bees (◊).
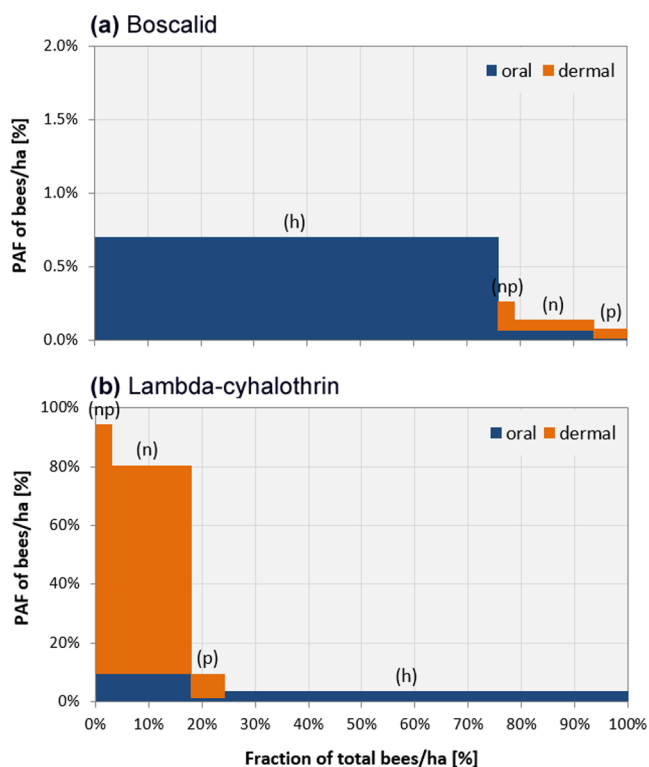
Fig. 5. Contribution of oral and dermal exposure to the potentially affected fraction (PAF) of bees as a function of the number of each bee type for (a) boscalid and (b) lambda-cyhalothrin, with p = pollen foragers, n = nectar foragers; np = nectar foragers in contact with pollen; h = bees inside the hive.

pesticide residue data in different matrices (pollen, nectar, leaves, etc.) and analyzed potential correlations to understand pesticide distribution patterns and exposure of honey bees. However, the limited availability of crop-specific measured residual concentrations in pollen and nectar and their high variability depending on the crop species and the specific conditions (Supplementary Information, Tables S9 and S10) represent a limitation for our study.

Another limitation is related to the actual pesticide application. To avoid the ecotoxicological effects of pesticides on honey bees, the application of insecticides in particular is often not allowed during the active flying hours of honey bees. However, residues can still contaminate nectar and pollen in sub-lethal doses, depending on physico-chemical properties of the pesticides, application method, and plant growth characteristics (Viik, 2012).

As outlined in Fig. 1, other pesticide-related exposure pathways than those considered are potentially relevant for honey bees. Our initial focus was on the predominant (oral exposure via pesticide residues in nectar) and most likely (dermal exposure via pesticide residues in pollen) pathways, considering especially potential exposure of individual types of forager honey bees, which represent 26% of the overall hive affected, while we did not differentiate the types of non-forager bees exposed to the collected contaminated pollen and nectar within the hive. Our characterization framework may be refined by exploring additional pathways, such as pathways relevant for in-hive exposure. This is specifically relevant, since the loss of forager honey bees may lead to adverse feedback on the development of the hives and the growth of larvae, and since this raises concerns about a potential global crisis for the agricultural industry and consumers. In this context, it would be crucial to better assess the exposure of honey bee larvae, which are fed with contaminated pollen and nectar brought by the foragers, provided that larvae-specific ecotoxicity data are available.

To consider ecotoxicity effects on bees, except for the assessment of toxicity effects in forager bees due to boscalid oral exposure where

chronic data were available, we used acute toxicity data based on 48 h exposure test duration (according to OECD guidelines for the testing of chemicals on honey bees) (OECD, 1998a, 1998b) as an approximation of effects from chronic or sub-chronic exposures for adult bees. In fact, acute data assess the immediate effects of chemical exposure and are based on administering a single dose, while for sub-chronic and chronic effects multiple doses are administered over a longer period of time. The typical experimental duration for acute toxicity corresponds to 4% of a honey bee forager's life cycle, since the biological cycle of worker honey bees, including forager bees, is about 40 to 45 days in the active period (i.e. summer) (Tremolada et al., 2011). Chronic effects are even more relevant for larvae. Pesticide residues can also reach larvae, where they might be metabolized. Using acute data is therefore a limitation in assessments that consider a long-term perspective and hence require chronic effect data in bees to reflect life-time exposure.

Finally, to allow for aggregating results of our proposed framework with results from other impacts contributing to biodiversity loss, our bee impact characterization factors need to be translated into damages on ecosystem quality. For both pesticides analyzed in the case study, we calculated the PAF of honey bees, which is generally in line with eco-system damages expressed in Potentially Disappeared Fraction (PDF) of species (Fantke et al., 2018a). However, the PAFs obtained for honey bees refer to the fractions of affected individuals within a single species, whereas in current LCIA and other ecotoxicity characterization frameworks, PAF generally refers to an affected fraction of distinct species living in the same ecosystem (e.g. freshwater ecosystem). In addition, the influence of affected bee type on the overall functioning of the hive will have to be evaluated for damage level assessments.

4.3. Future research needs

To fully operationalize our proposed framework, further research is required.

Several rather conservative assumptions in our exposure estimates require further refinement based on additional research. This includes better accounting for differences in bee skin and honey sack membrane permeability as well as external body surface and honey sack surface fractions in contact with respectively nectar and pollen, but also degradation and transformation mechanisms in foragers and in-hive.

Nectar foragers represent the group of honey bees mostly affected by both studied pesticides, and it is important to consider both exposure and effects across all applied pesticides instead of focusing only on pesticides with high ecotoxicity potentials or modes of action specifically targeting insects. Further, our modeling framework needs to be extended to consider the wide range of pesticides applied in agriculture on the various crops that are relevant for insect pollinators, accounting for the different application contexts (e.g. method of application, treatment outside the flowering seasons, application frequency) and spatial granularity in environmental conditions (e.g. climate, field size). In this context, field effects, such as buffer zones, wild flower patches and field margins, on the variety and number of pollinators need to be considered (Le Féon et al., 2013; Nicholls and Altieri, 2013). For extending our framework, it is crucial to obtain pollen and nectar residue data, namely concentrations as well as dissipation half-lives linked to the mass of the various pesticide applied to the different crops. If concentration and dissipation data are rare, they can either be directly measured or extrapolated from residue data in other plant components, or other estimation approaches should be explored (EFSA, 2013; Fantke and Juraske, 2013; Fantke et al., 2014), which equally applies when chronic ecotoxicity data are not available and need to be estimated by applying an acute-to-chronic extrapolation as available for freshwater ecotoxicity (Aurisano et al., 2019; Henderson et al., 2011; Posthuma et al., 2019). For refining our framework, larvae-specific data and a more detailed mass balance of the pesticide residues in the different crop-environment systems will be needed.

In a broader sense, linking pesticide use to the capacity of hives to

handle exposure to pesticides in a sustainable manner would put our characterization framework also in the context of absolute environmental sustainability limits for chemicals in line with the global sustainable development agenda (Fantke and Illner, 2019). In this perspective, it is important to also consider the wider realm of insect pollinators and their specific characteristics, evaluate cumulative effects of pollinators simultaneously foraging on multiple crops and thus being exposed to a multitude of pesticides, and also assess other sources than pesticides contributing to worldwide pollinator decline, for which our framework constitutes a suitable starting point.

More detailed pesticide emission information is increasingly becoming available. Higher-tier models, such as BEEHAVE (Becher et al., 2014), might be explored to couple such information with increased ecological realism. Possible starting points could be to vary only pesticide-related aspects while keeping all other aspects constant, or to parameterize complex interactions in the hive.

Finally, insect pollination contributes to important ecosystem services. Hence, it might be relevant to quantify the impact of pollinators decline on ecosystem services (Koellner et al., 2013). However, linking our impact results associated with pesticide exposure to ecosystem services requires not only the consideration of additional stressors affecting pollinators, but also their association with the different ecosystem functions.

5. Conclusion

We proposed an impact characterization framework that constitutes a first step toward operationally integrating exposure of honey bees to pesticides and related effects in comparative chemical alternatives assessments, chemical prioritization and LCIA methods. Using honey bees as most relevant pollinator species, we defined bee intake and dermal contact fractions as novel metrics representing respectively oral and dermal exposure per unit mass applied, and tested our framework on two pesticides applied to oilseed rape in Europe. Results of our case study showed that exposure varies between types of forager bees, with highest dermal contact fraction of 59 ppm in nectar foragers for lambda-cyhalothrin, and highest intake fractions of 32 and 190 ppm in nectar foragers for boscalid and lambda-cyhalothrin, respectively. In-hive oral exposure is up to 115 times higher than forager oral exposure. The total impacts, derived as combination of exposure and effects, are three orders of magnitude higher for lambda-cyhalothrin. Overall, nectar foragers are the most affected forager type for both pesticides, dominated by oral exposure.

The outcomes demonstrate the significant value of integrating impacts associated with insect pollinator exposure to pesticides in LCIA methods and chemical substitution and prioritization frameworks. Our framework is initially developed for honey bees. However, while distinct behavior and life cycle across pollinating insect species might lead to differences in exposure and effects (Sgolastra et al., 2019), the mass balance basis and comparative nature of our framework render it a suitable starting point to evaluate pesticide-related impacts on different pollinator species.

Overall, our framework should be expanded to cover all relevant pesticide-crop combinations and other possibly relevant exposure pathways and pollinator species, in order to guide decisions related to the identification and replacement of potentially harmful pesticides for pollinating insects.

Author contributions

ECr, SS and PF designed the study. ECr, OJ and PF developed the methodological framework and visualized the data. ECr conducted the formal analysis, ECo validated the data. ECr wrote the original draft. PF, OJ, ECo and SS reviewed and edited the manuscript. PF provided overall guidance.

Declaration of Competing Interest

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

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.105642.

References

Arnold, G., Pistorius, J., Steeger, T., Thompson, H., 2012. Statement on the findings in recent studies investigating sub-lethal effects in bees of some neonicotinoids in consideration of the uses currently authorised in Europe. EFSA J. 10, 2752–2779.

Aurisano, Nicolò, Albizzati, Paola, Hauschild, Michael, Fantke, Peter, 2019. Extrapolation factors for characterizing freshwater ecotoxicity effects. Environ. Toxicol. Chem. 38, 2568–2582. https://doi.org/10.1002/etc.4564.

Barmaz, S., Vaj, C., Ippolito, A., Vighi, M., 2012. Exposure of pollinators to plant protection products. Ecotoxicology 21, 2177–2185. https://doi.org/10.1007/s10646-012-0971-7.

Baveco, J.M., Focks, A., Belgers, D., van der Steen, J.J., Boesten, J.J., Roessink, I., 2016. An energetics-based honeybee nectar-foraging model used to assess the potential for landscape-level pesticide exposure dilution. Peer J. 4, e2293. https://doi.org/10.7717/peerj.2293.

Becher, M.A., Grimm, V., Thorbek, P., Horn, J., Kennedy, P.J., Osborne, J.L., 2014. BEEHAVE: a systems model of honeybee colony dynamics and foraging to explore multifactorial causes of colony failure. J. Appl. Ecol. 51, 470–482. https://doi.org/10.1111/1365-2664.12222.

Bennett, D.H., Margni, M.D., McKone, T.E., Jolliet, O., 2002. Intake fraction for multimedia pollutants: a tool for life cycle analysis and comparative risk assessment. Risk Anal. Int. J. 22, 905–918. https://doi.org/10.1111/1539-6924.00260.

Bohart, G.E., Nye, W.P., 1956. Bees. Foraging for nectar and pollen. Glean. Bee Cult. 84, 602.

Bonmatin, J.M., Giorioo, C., Girolami, V., Goulson, D., Kreutzweiser, D.P., Krupke, C., Liess, M., Long, E., Marzaro, M., Mitchell, E.A.D., Noome, D.A., Simon-Delso, N., Tapparo, A., 2015. Environmental fate and exposure; neonicotinoids and fipronil. Environ. Sci. Pollut. Res. 22, 35–67. https://doi.org/10.1007/s11356-014-3332-7.

Choudhary, A., Sharma, D.C., 2008. Dynamics of pesticide residues in nectar and pollen of mustard (Brassica juncea (L.) Czern.) grown in Himachal Pradesh (India). Environ. Monit. Assess. 144, 143–150. https://doi.org/10.1007/s10661-007-9952-3.

Christopher Cutler, G., Scott-Dupree, C.D., 2007. Exposure to clothianidin seed-treated canola has no long-term impact on honey bees. J. Econ. Entomol. 100, 765–772. https://doi.org/10.1093/jee/100.3.765.

Crenna, E., Sala, S., Polce, C., Collina, E., 2017. Pollinators in life cycle assessment: towards a framework for impact assessment. J. Clean. Prod. 140, 525–536. https://doi.org/10.1016/j.jclepro.2016.02.058.

Doucette, W.J., Shunthirasingham, C., Dettenmaier, E.M., Zaleski, R.T., Fantke, P., Arnot, J.A., 2018. A review of measured bioaccumulation data on terrestrial plants for organic chemicals: metrics, variability, and the need for standardized measurement protocols. Environ. Toxicol. Chem. 37, 21–33. https://doi.org/10.1002/etc.3992.

EC-JRC (European Commission, Joint Research Centre), 2011. Recommendations based on existing environmental impact assessment models and factors for life cycle assessment in European context. Publications Office of the European, Luxembourg.

EFSA (European Food Safety Authority), 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA J. 11, 3295–3563.

EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment of the active substance lambda-cyhalothrin. EFSA J. 12, 3677.

EFSA (European Food Safety Authority), 2018. Draft renewal assessment report under regulation (EC) 1107/2009 – Boscalid: List of endpoint. Report. Available at: http://www.efsa.europa.eu/en/consultations/call/190125.

Fantke, P., Jolliet, O., 2016. Life cycle human health impacts of 875 pesticides. Int. J. Life Cycle Assess. 21, 722–733. https://doi.org/10.1007/s11367-015-0910-y.

Fantke, P., Aurisano, N., Bare, J., Backhaus, T., Bulle, C., Chapman, P.M., De Zwart, D., Dwyer, R., Ernstoff, A., Golsteijn, L., Holmquist, H., Jolliet, O., McKone, T.E., Owsianiak, M., Peijnenburg, W., Posthuma, L., Roos, S., Saouter, E., Schowanek, D., van Straalen, N.M., Vijver, M.G., Hauschild, M., 2018a. Toward harmonizing

ecotoxicity characterization in life cycle impact assessment. Environ. Toxicol. Chem. 37, 2955–2971. https://doi.org/10.1002/etc.4261.

Fantke, P., Aylward, L., Bare, J., Chiu, W.A., Dodson, R., Dwyer, R., et al., 2018b. Advancements in life cycle human exposure and toxicity characterization. Environ. Health Perspect. 126, 125001. https://doi.org/10.1289/EHP3871.

Fantke, P., Gillespie, B.W., Juraske, R., Jolliet, O., 2014. Estimating half-lives for pesticide dissipation from plants. Environ. Sci. Technol. 48, 8588–8602. https://doi.org/10.1021/es500434p.

Fantke, P., Illner, N., 2019. Goods that are good enough: Introducing an absolute sustainability perspective for managing chemicals in consumer products. Curr. Opin. Green Sustain. Chem. 15, 91–97. https://doi.org/10.1016/j.cogsc.2018.12.001.

Fantke, P., Juraske, R., 2013. Variability of pesticide dissipation half-lives in plants. Environ. Sci. Technol. 47, 3548–3562. https://doi.org/10.1021/es303525x.

FAO (Food and Agriculture Organization of the United Nations), 2016. A Scheme and Training Manual on Good Agricultural Practices (GAP) for Fruits and Vegetables Volume 1 The scheme – standard and implementation infrastructure.

Fischer, D., Moriarty, T. (Eds.), 2014. Pesticide Risk Assessment for Pollinators. Society of Environmental Toxicology and Chemistry (SETAC) & Wiley Blackwell https://doi.org/10.1002/9781118852408.

Gierer, F., Vaughan, S., Slater, M., Thompson, H.M., Elmore, J.S., Girling, R.D., 2019. A review of the factors that influence pesticide residues in pollen and nectar: future research requirements for optimising the estimation of pollinator exposure. Environ. Pollut. 249, 236–247. https://doi.org/10.1016/j.envpol.2019.03.025.

Goulson, D., Nicholls, E., Botías, C., Rotheray, E.L., 2015. Bee declines driven by combined stress from parasites, pesticides, and lack of flowers. Science 347, 1255957. https://doi.org/10.1126/science.1255957.

He, L.M., Troiano, J., Wang, A., Goh, K., 2008. Environmental chemistry, ecotoxicity, and fate of lambda-cyhalothrin. In: Whitacre, D.M. (Ed.), Reviews of Environmental Contamination and Toxicology. Springer, New York, NY.

Henderson, A.D., Hauschild, M.Z., van de Meent, D., Huijbregts, M.A.J., Larsen, H.F., Margni, M., McKone, T.E., Payet, J., Rosenbaum, R.K., Jolliet, O., 2011. USEtox fate and ecotoxicity factors for comparative assessment of toxic emissions in life cycle analysis: sensitivity to key chemical properties. Int. J. Life Cycle Assess. 16, 701. https://doi.org/10.1007/s11367-011-0294-6.

IPBES, 2016. Summary for policymakers of the assessment report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on pollinators, pollination and food production. Secretariat of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services, Bonn, Germany.

Johnson, R.M., Ellis, M.D., Mullin, C.A., Frazier, M., 2010. Pesticides and honey bee toxicity–USA. Apidologie 41, 312–331. https://doi.org/10.1051/apido/2010018.

Kasiotis, K.M., Anagnostopoulos, C., Anastasiadou, P., Machera, K., 2014. Pesticide residues in honeybees, honey and bee pollen by LC–MS/MS screening: reported death incidents in honeybees. Sci. Total Environ. 485, 633–642. https://doi.org/10.1016/j.scitotenv.2014.03.042.

Kim, S., Thiessen, P.A., Bolton, E.E., Chen, J., Fu, G., Gindulyte, A., Han, L., He, J., He, S., Shoemaker, B.A., Wang, J., Yu, B., Zhang, J., Bryant, S.H., 2015. Pubchem substance and compound databases. Nucleic Acids Res. 44, D1202–D1213. https://doi.org/10.1093/nar/gkv951.

Klein, M., 2012. Estimation of reasonable application dates dependent on BBCH crop development stages for FOCUS PELMO. (Fraunhofer-Institut, Molekularbiologie und Angewandte Ökologie, 2012). AppDate 2.0.

Koellner, T., De Baan, L., Beck, T., Brandão, M., Civit, B., Margni Milà i Canals, L., Saad, R., Maia de Souza, D., Müller-Wenk, R., 2013. UNEP-SETAC guideline on global land use impact assessment on biodiversity and ecosystem services in LCA. Int. J. Life Cycle Assess. 18, 1188–1202. https://doi.org/10.1007/s11367-013-0579-z.

Krupke, C.H., Hunt, G.J., Eitzer, B.D., Andino, G., Given, K., 2012. Multiple routes of pesticide exposure for honey bees living near agricultural fields. PLoS One 7, e29268. https://doi.org/10.1371/journal.pone.0029268.

Le Féon, V., Burel, F., Chifflet, R., Henry, M., Ricroch, A., Vaissière, B.E., Baudry, J., 2013. Solitary bee abundance and species richness in dynamic agricultural landscapes. Agric. Ecosyst. Environ. 166, 94–101. https://doi.org/10.1016/j.agee.2011.06.020.

Neumann, P., Carreck, N.L., 2010. Honey bee colony losses. J. Apic. Res. 49, 1–6. https://doi.org/10.3896/IBRA.1.49.1.01.

Nicholls, C.I., Altieri, M.A., 2013. Plant biodiversity enhances bees and other insect pollinators in agroecosystems. A review. Agron. Sustain. Dev. 33, 257–274. https://doi.org/10.1007/s13593-012-0092-y58.

OECD (Organisation for Economic Co-operation and Development), 1998a. OECD guidelines for the testing of chemical – Test No. 214: Honey bees Acute Contact Toxicity Test. 7.

OECD (Organisation for Economic Co-operation and Development), 1998b. OECD guidelines for the testing of chemical – Test No. 213: Honey bees Acute Oral Toxicity Test. 8.

Poquet, Y., Bodin, L., Tchamitchain, M., Fusellier, M., Giroud, B., Lafay, F., Buleté, A., Tchamitchain, S., Cousin, M., Pélissier, M., Brunet, J.-L., Belzunces, L.P., 2014. A pragmatic approach to assess the exposure of the honey bee (Apis mellifera) when subjected to pesticide spray. PLoS One 9, e113728. https://doi.org/10.1371/journal.pone.0113728.

Posthuma, L., van Gils, J., Zijp, M.C., van de Meent, D., de Zwart, D., 2019. Species sensitivity distributions for use in environmental protection, assessment, and management of aquatic ecosystems for 12 386 chemicals. Environ. Toxicol. Chem. 38, 905–917. https://doi.org/10.1002/etc.4373.

Potts, S.G., Biesmeijer, J.C., Kremen, C., Neumann, P., Schweiger, O., Kunin, W.E., 2010. Global pollinator declines: trends, impacts and drivers. Trends Ecol. Evol. 25 (6), 345–353. https://doi.org/10.1016/j.tree.2010.01.007.

PPDB (Pesticide Properties DataBase), 2019. https://sitem.herts.ac.uk/aeru/ppdb/ (accessed June 2018).

PRBKA (Pinner & Ruislip Beekeeper's Association), 2018. Outside Bees, Food and Foragers. http://www.prbka.co.uk/?page_id=1611 (accessed June 2018).

Robinson, G.E., 1992. Regulation of division of labor in insect societies. Annu. Rev. Entomol. 37, 637–665. https://doi.org/10.1146/annurev.en.37.010192.003225.

Rortais, A., Arnold, G., Halm, M.-P., Touffet-Briens, F., 2005. Modes of honeybees exposure to systemic insecticides: estimated amounts of contaminated pollen and nectar consumed by different categories of bees. Apidologie 36, 71–83. https://doi.org/10.1051/apido:2004071.

Rortais, A., Arnold, G., Dourne, J.-L., More, S.J., Sperandio, G., Streissl, F., Szentes, C., Verdonck, F., 2017. Risk assessment of pesticides and other stressors in bees: principles, data gaps and perspectives from the European Food Safety Authority. Sci. Tot. Environ. 587, 524–537. https://doi.org/10.1016/j.scitotenv.2016.09.127.

Rosenbaum, R.K., Anton, A., Bengoa, X., Bjørn, A., Brain, R., Bulle, C., et al., 2015. The Glasgow consensus on the delineation between pesticide emission inventory and impact assessment for LCA. Int. J. Life Cycle Assess. 20, 765–776. https://doi.org/10.1007/s11367-015-0871-1.

Rueppell, O., Kennedy, A., 2019. Aging and behavior in honey bees. In: Encyclopedia of Animal Behavior (Second Edition), pp. 709–715 ISBN: 9780128132524.

Sanchez-Bayo, F., Goka, K., 2014. Pesticide residues and bees–a risk assessment. PLoS One 9, e94482. https://doi.org/10.1371/journal.pone.0094482.

Sanchez-Bayo, F., Goka, K., 2016. Impacts of pesticides on honey bees. In: Chambo (Ed.), Beekeeping and Bee Conservation: Advances in Research, pp. 77–97 https://doi.org/10.5772/62487.

Sgolastra, F., Hinarejos, S., Pitts-Singer, T.L., Boyle, N.K., Joseph, T., Lŭckmann, J., Raine, N.E., Singh, R., Williams, N.M., Bosch, J., 2019. Pesticide exposure assessment paradigm for solitary bees. Environ. Entomol. 48, 22–35. https://doi.org/10.1093/ee/nvy105.

Seeley, T.D., 1995. The Wisdom of the Hive Cambridge. Belknap Press of Harvard University Press, MA.

Shin, H.-M., Ernstoff, A., Arnot, J.A., Wetmore, B.A., Csiszar, S.S., Fantke, P., Zhang, X., McKone, T.E., Jolliet, O., Bennett, D.H., 2015. Risk-based high-throughput chemical screening and prioritization using exposure models and in vitro bioactivity assays. Environ. Sci. Technol. 49, 6760–6771. https://doi.org/10.1021/acs.est.5b00498.

Simon-Delso, N., San Martin, G., Bruneau, E., Hautier, L., 2018. Time-to-death approach to reveal chronic and cumulative toxicity of a fungicide for honeybees not revealed with the standard ten-day test. Sci. Rep. 8, 7241. https://doi.org/10.1038/s41598-018-24746-9.

Simon-Delso, N., San Martin, G., Bruneau, E., Hautier, L., Medrzycki, P., 2017. Toxicity assessment on honey bee larvae of a repeated exposition of a systemic fungicide, boscalid. Bull. Insectol. 70, 83–90.

Sponsler, D.B., Johnson, R.M., 2017. Mechanistic modeling of pesticide exposure: the missing keystone of honey bee toxicology. Environ. Toxicol. Chem. 36, 871–881. https://doi.org/10.1002/etc.3661.

Steingrímsdóttir, M.M., Petersen, A., Fantke, P., 2018. A screening framework for pesticide substitution in agriculture. J. Clean. Prod. 192, 306–315. https://doi.org/10.1016/j.jclepro.2018.04.266.

Syngenta, 2018. Hallmark Zeon – product label. Available at: https://www.syngenta.co.uk/sites/g/files/zhg151/f/hallmark_0595_2017.pdf (Accessed February 2020).

Thompson, H.M., 2012. Interaction Between Pesticides and Other Factors in Effects on Bees. EFSA Support. Publ.

Tremolada, P., Bernardinelli, I., Rossaro, B., Colombo, M., Vighi, M., 2011. Predicting pesticide fate in the hive (part 2): development of a dynamic hive model. Apidologie 42, 439–456. https://doi.org/10.1007/s13592-011-0012-1.

USEPA (United States Environmental Protection Agency), 2014. Guidance for Assessing Pesticide Risks to Bees.

Van der Zee, R., Pisa, L., Andonov, S., Brodschneider, R., Charrière, J.D., Chlebo, R., et al., 2012. Managed honey bee colony losses in Canada, China, Europe, Israel and Turkey, for the winters of 2008–9 and 2009–10. J. Apic. Res. 51, 100–114. https://doi.org/10.3896/IBRA.1.51.1.12.

Viik, E., 2012. The Impact of Spring Oilseed Rape Fertilization and Pesticide Application on Bees (Apoidea). Doctoral dissertation.

Villa, S., Vighi, M., Finizio, A., Serini, G.B., 2000. Risk assessment for honeybees from pesticide-exposed pollen. Ecotoxicology 9, 287–297. https://doi.org/10.1023/A:1026522112328.

Wallner, K., 2009. Sprayed and seed dressed pesticides in pollen, nectar and honey of oilseed rape. In: Hazards of Pesticides to Bees – 10th International Symposium of the ICP-Bee Protection Group Julius-Kühn-Archiv, pp. 152–153.

Watson, K., Stallins, J.A., 2016. Honey bees and colony collapse disorder: a pluralistic reframing. Geogr. Compass 10, 222–236. https://doi.org/10.1111/gec3.12266.

Westcott, L., Nelson, D., 2001. Canola pollination: an update. Bee World 82, 115–129. https://doi.org/10.1080/0005772X.2001.11099514.

Williams, I.H., 2010. The major insect pests of oilseed rape in europe and their management: an overview. In: Williams, I. (Ed.), Biocontrol-Based Integrated Management of Oilseed Rape Pests. Springer, Dordrecht.

Woodcock, B.A., Bullock, J.M., Shore, R.F., Heard, M.S., Pereira, M.G., Redhead, J., Ridding, L., Dean, H., Sleep, D., Henrys, P., Peyton, J., Hulmes, S., Hulmes, L., Sárospataki, M., Saure, C., Edwards, M., Genersch, E., Knäbe, S., Pywell, R.F., 2017. Country-specific effects of neonicotinoid pesticides on honey bees and wild bees. Science 356, 1393–1395. https://doi.org/10.1126/science.aaa1190.