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# A review of the effects of agricultural intensification and the use of pesticides on honey bees and their products and possible palliatives

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## Abstract

There is considerable scientific evidence revealing a decrease in pollinating insects in different ecosystems around the world. In this context, agricultural intensification and the use of phytosanitary products are likely the main causes. This problem is common to many pollinators but of particular ecosystemic, economic and bromatological significance for honey bees (*Apis mellifera*) since their presence in these landscapes is mainly due to the proximity of apiaries for human food production and because they are the most important biotic pollinators of agricultural crops. In this review, we present a synthesis of the results of several years of research on this topic, as well as potential solutions referenced in the bibliography that might help alleviate the effects of contamination on honey bees and their products. Additionally, we expose the possible limits of the real implementation of such solutions and conclude on the need to implement land-use planning strategies for agricultural systems. Without mitigating actions in the short term, the sustainability of agricultural ecosystems as bee-friendly habitats and the production of foods suitable for human consumption are uncertain.

**Additional key words:** territorial management; bee stressors; crop management; glyphosate; biotic pollinators; *Apis mellifera*.

**Abbreviation used:** CCD (Colony Collapse Disorder); MRL (Maximum Residue Levels).

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# Introduction

The world's population is growing rapidly, having tripled since 1950 to a current total of 7.6 billion, and all evidence points towards the fact that, far from maintaining this number, it will presumably increase to 9.6 billion by 2050 (Population Reference Bureau, 2017). The future scenario is truly uncertain, since such a demographic explosion has never been recorded in human history. In this context, global food stocks may be halved by 2050 (Laio *et al*., 2016). This estimation is based on several factors: the land area likely to be affected by agricultural production is finite, currently more than a third of the overall area is used for agricultural purposes (Foley *et al*., 2005; Klein Goldewijk *et al*., 2011), and increasing it will transform landscapes with undesirable environmental and social consequences such as the destruction of forests (Ramankutty & Foley, 1999). In addition, population growth will promote urban expansion causing destruction of natural areas and fragmentation of the landscape in general, and a reduction of some of the most productive agricultural lands in the world (Seto *et al*., 2012). Consequently, this phenomenon produces social, political, and economic changes that the global agricultural matrix cannot escape.

Evidently, the immediate future will be inextricably linked to a progressive process of agricultural intensification, defined as the set of practices that increase productivity per unit area. This increase in agricultural productivity should also be proportional to the population increase, given the improvement in the average human food quality that has been happening well in recent decades (FAOSTAT, 2017). To a large extent, this agronomic feat has involved a greater use of agrochemichals by the use of agrochemicals or pesticides that protect crops from a significant number of pests, weeds and/or diseases (Zhang *et al*., 2011; Atwood & Paisley-Jones, 2017). Moreover, the application of pesticides has not only increased agricultural productivity and crop yield, but has also contributed to making food more affordable and occasionally to increase farmers' incomes (at least in the short term), although in the long term the volume and number of pesticides required increase due to herbicide-resistant weeds (Antonini & Argilés-Bosch, 2017).

The transformation of landscapes by anthropic actions (linked to population increase and progressive improvement in food quality) is of such magnitude that there are almost no virgin environments that escape the effects of agricultural intensification (Chhabra *et al*., 2006; Liu *et al*., 2014) and consequently to chemical contamination. Understanding this problem in its real dimension is the only way to enable resilient and sustainable social-productive development (UN-FAO, 2017).

In the context of agricultural intensification and mass use of agrochemicals, exposure to non-target organisms is unfortunately inevitable (Gierer *et al*., 2019). In fact, in any agricultural application of agrochemicals (foliar spraying or topical seed treatments), only a small proportion of the product used (generally less than 5%) will actually accomplish the goal of preventing, destroying, repelling, attracting or controlling pests, including unwanted species of plants or animals (FAO-WHO, 1997; Goulson, 2014; Yamada, 2017). The remaining pesticide (*i.e*., 95%) will be distributed to water and soil where, depending on individual chemical properties, it will be altered by environmental factors over a potentially long period of time (Goulson, 2014).

Honey bees are a clear example of non-target organisms unintentionally reached by agrochemicals (Sgolastra *et al*., 2018; Azpiazu *et al*., 2021). In this sense, the scientific literature mentions multiple routes for the exposure of honey bees to pesticides, either directly by spraying the flowers, by treated seeds, by contaminated water, by inhalation and/or contact of pesticides sprayed or indirectly by accumulation in all plant tissues, including nectar, pollen and other plant exuded (Böhme *et al*., 2017). Indeed, although without confirmatory evidence, they are considered particularly susceptible to pollutant exposure (Arena & Sgolastra, 2014), and, as a result, they are considered one of the best environmental health bioindicators currently available (Rapisarda & Hussein, 2002; De Oliveira *et al*., 2016). In other words, if bees in a given region are healthy and do not show signs of contamination, it can be supposed that the surrounding environment is relatively detoxified. On the contrary, environmental pollution will surely be reflected in analyses that are performed on bees or their products. Thus, the aim of the present work was to provide an in-depth review and critical analysis of the implications of these facts, and a proposition to address these issues by means of territorial management.

# Methodology

This manuscript is framed as a critical review (Grant & Booth, 2009), in which several topics related to the effects of agricultural intensification and the use of pesticides on honey bees are addressed. To this end, we performed a search in Web of Science®, Scopus®, PubMed Central® and Scielo databases, using the following search string: ("bee" OR "honey" OR "pollen" OR "pollination") AND ("pesticide" OR "agricultural intensification" OR "agricultural management"). We found 6490 documents in Web of Science®, 3177 documents in Scopus®, 960 documents in PubMed Central®, and only 18 documents in Scielo. We then checked for duplicates and selected scientific articles (including original studies and reviews) and technical reports that discussed the lethal and sublethal effects of pesticides on honey bees. Undergraduate thesis, scientific dissemination reports and abstracts in conferences were excluded from the review. Emphasis was placed on articles published in the past 15 years, although older publications were also considered (particularly for the introduction) resulting in 87 unique scientific articles indexed on Web of Science®. Details about the publication date, citation count and country of origin are summarized in Fig. 1, by using the software referenced by Van Eck & Waltman (2014). This review presents, analyses, and synthesizes the most salient findings on the topic within these sources, and concludes with a new proposal to address the encountered issues based on territorial management.

# Main stressors for bees

Although agricultural intensification and pesticide pollution are undoubtedly largely responsible for reducing the abundance and diversity of bees and other insects in different ecosystems around the world (Sanchez-Bayo & Wyckhuys, 2019), it is necessary to consider that there are many other stressors affecting bees (Goulson *et al*., 2015). In this sense, stressors can be grouped into four types (Rortais *et al*., 2017), however it is important to remember that its effects are usually interrelated (Fig. 2), being both additive and synergistic (Belsky & Joshi, 2019):

**1) Environmental stressors,** which strongly condition bees' survival. Examples of such stressors are climate change, habitat destruction, construction of roads and cities, etc (Goulson *et al*., 2015). The greatest negative impact of this type of stressor is suffered by non-*Apis* (wild) bees that have seen their populations decimated because their nesting sites and natural food sources are reduced (Winfree *et al*., 2011, Kiatoko *et al.,* 2017). On the other

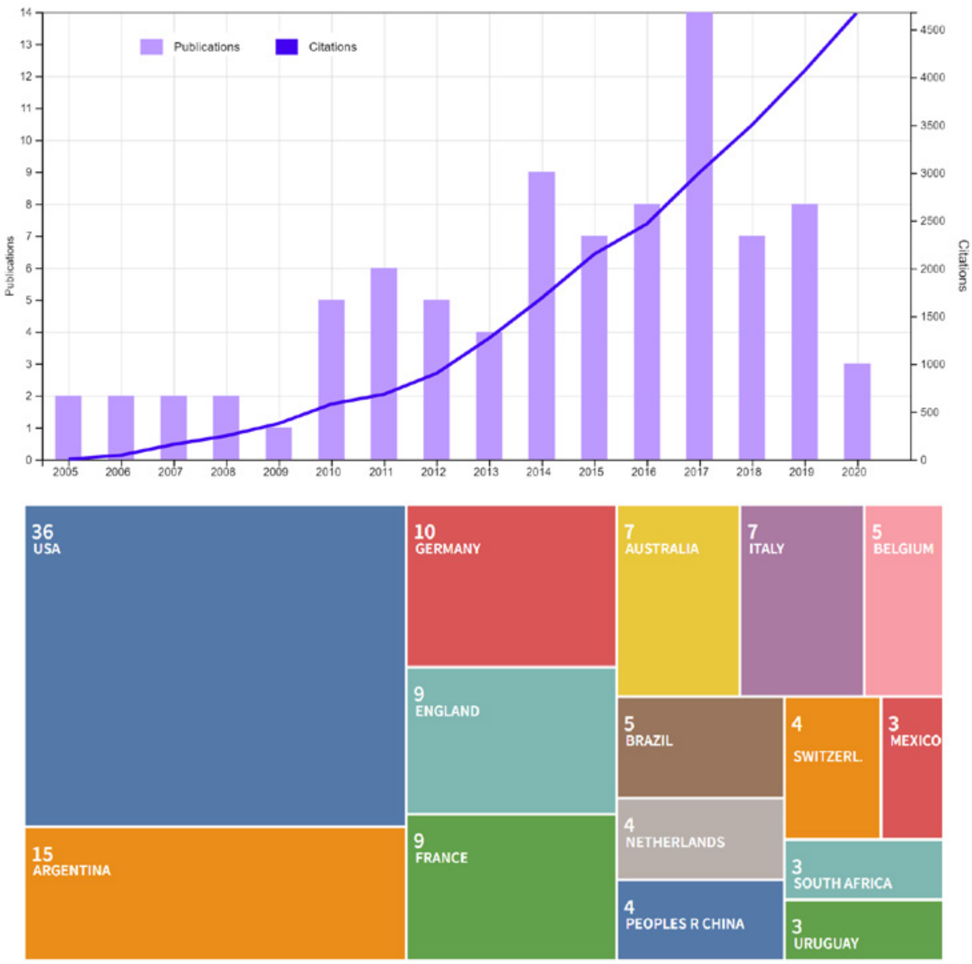


**Figure 1**. Number of publications per year (violet bars, top graph), citation count (blue line, top graph) and country of origin (bottom graph) corresponding to the selected publications, indexed in Web of Science® (n=87).

hand, *Apis mellifera* bees (mostly managed for productive purposes) have possibly coped a little better with this type of stressor, since *inter alia*, nesting sites are provided by the beekeeper. Additionally, food sources of *A. mellifera*, reduced by environmental stressors, are compensated for by artificial feeding and/or transhumance of the apiaries (Olate-Olave *et al*., 2021).

**2) Biological stressors,** which include pests and diseases of bees, such as varroosis (ectoparasite), foulbrood (bacteria), *Nosema* (microsporidian fungus), and viral diseases, among others. Some of these are sporadic in apiaries of *A. mellifera*, while others such as varroasis (a disease caused by *Varroa destructor*) can be considered endemic since they are present almost all over the world (Bernardi &Venturino, 2016).

**3) Nutritional stressors,** that are linked to the bees' food sources, are caused by the limited diversity of sources of protein (pollen) or carbohydrates (nectar) and/or by imbalances in the intake of lipids, sugars, vitamins, and minerals (Vaudo *et al*., 2015). Many of these nutritional deficiencies and imbalances are the result of the increase in the area allocated to agricultural production (Di Pasquale *et al*., 2013), that leads to the replacement of many species with and different flowering times by only one species (that only occasionally presents flowers that are attractive to bees) or by species that only supply pollen, such as anemophilous crops (maize, sorghum, rice, wheat, etc.).

**4) Chemical stressors,** which include mainly xenobiotic compounds, often derived from agriculture, but also contaminants from urban pollution, industrial waste, inappropriate health management of hives, gardening, etc., as well as harmful natural compounds, such as mycotoxins, plant alkaloids, different secretions of insects, among others. This broad set is one of the most pressing problems for pollinating insects in general (Powney *et al*., 2019) and possibly for honey bees in particular, since their genome is significantly deficient in the number of genes encoding detoxification enzymes (Claudianos *et al*., 2006). This remarkable difference makes honey bees possibly they are susceptible to pesticides than other insects, although some authors question this possibility (Hardstone & Scott, 2010).

The complexity of the problem lies in the fact that this broad set of stressors do not operate independently (Brook

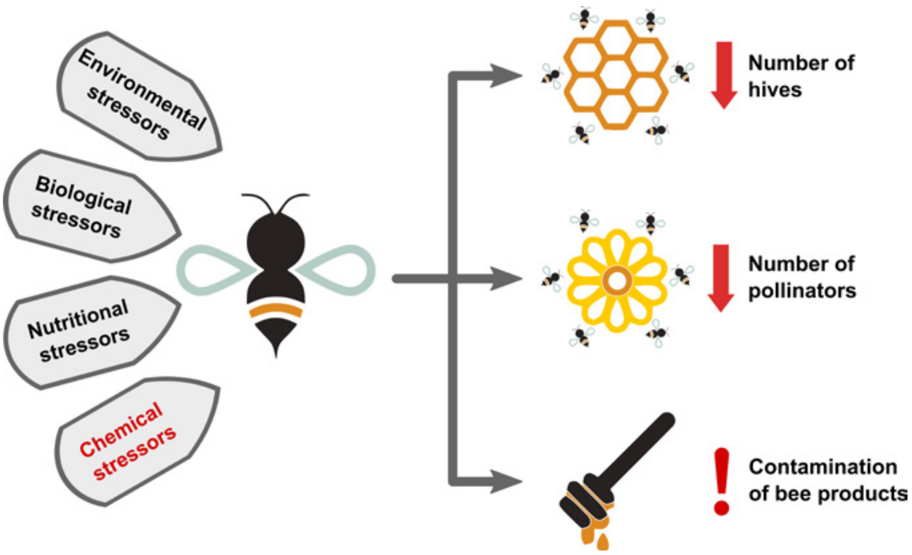


**Figure 2**. Effects of environmental, biological, nutritional and chemical stressors on honey bees and their products.

*et al*., 2008). On the contrary, all of them interact with each other and, consequently, their impact on bee populations is unlikely to be reversed unless there is a coordinated intervention against all of them.

# Pesticides and honey bees

## Pesticide contamination: localized or widespread issue?

The presence of pesticides in honey bees, honey, pollen, and wax has been reported as a worldwide issue (Chauzat *et al*., 2011; Mitchell *et al*., 2017), as well as in specific regions and countries, *e.g*. North America (Mullin *et al*., 2010), Belgium (Ravoet *et al*., 2015; Agrebi *et al*., 2020), Kenya (Irungu *et al*. 2016), Argentina (Medici *et al*., 2019), Uganda (Amulen *et al*., 2017), Mexico (Valdovinos-Flores *et al*., 2017) and in the Seychelles Islands (Muli *et al*., 2018).

The presence of pesticides in hives is closely related to the surrounding environment (García-Chao *et al*., 2010; Mullin *et al*., 2010; Chauzat *et al*., 2011; Panseri *et al*., 2014; Malhat *et al*., 2015), particularly when this environment is used for agriculture (Kremen *et al*., 2002; Biesmeijer *et al*., 2006; Potts *et al*., 2010a; Gleiciani Bürger & Campos, 2014).

## Damage on managed hives, complexity and interpretation of loss of hives

Assessing the impact of pesticides and agricultural intensification on managed hives of *A. mellifera* is a difficult task, given that it develops almost all over the world, with a wide range of climates, landscapes, vegetation, etc. and fundamentally with different types of beekeepers who own from a few to thousands of colonies, and manage hives both as a business or as a hobby (Vandame & Palacio, 2010). Thus, bringing together the most recent published scientific evidence, which addresses the risk of agricultural pesticides to honey bees and their products for human consumption from different approaches, is especially relevant because it contributes to informed decision-making. In this regard, reports of a decrease or disappearance in the number of hives around the world (often labelled as Colony Collapse Disorder or CCD) are widely known and referred widely in the scientific literature (Van Engelsdorp *et al*., 2017). However, the real causes of this event do not have the same level of agreement in the scientific community, although the consensus in characterizing this phenomenon is to attribute it to multiple causes (Van Engelsdorp *et al*., 2009), among which are agricultural pesticides (Watson & Stallins, 2016).

Currently, US beekeepers lose approximately 40% of their colonies each year, although with important variations between the different states (Kulhanek *et al*., 2017), while annual losses of approximately 30% are reported for Europe and South Africa (Pirk *et al*., 2014) and 3–13% in China, both for *A. mellifera* and *Apis cercana* (Chen *et al*., 2017). Argentina estimates an average loss of 30% of colonies per year (Maggi *et al*., 2016), which means the annual death of about 840,000 hives compared to the country's 2.8 million registered hives (Gallacher & Justo, 2016). These percentages merit some considerations due to their magnitudes: the death of managed hives, particularly during the winter season, is a completely normal phenomenon, contemplated by beekeepers and implicit in the activity. Obviously, 30 or 40 % is a very high number, yet every year beekeepers, with different agronomic practices, replenish these losses in good proportion (Genersch *et al*., 2010). In fact, the number of managed honey bee colonies has increased over the last decade (Aizen *et al*., 2009; Steinhauer *et al*., 2018). This simple clarification (the winter mortality of managed honey bees is a normal phenomenon and that beekeepers compensate with different hive multiplication techniques) is not always present in published studies and leads, in many cases, hasty conclusions and incorrect sizing of the problem.

As previously stated, the causes of these high losses are very diverse, and although it is not only a result of agricultural intensification and pesticide use, but these are also two powerful factors surely involved in the high reported mortality rates. Recent research suggests that some consequences of agricultural intensification observed in bees, especially nutritional limitation for reduction of floral supply (Foley *et al.,* 2012), and exposure to sub-lethal doses of pesticides (Wu *et al*., 2012), induce immune suppression in *A. mellifera*, which in time makes it difficult for bees to defend against the increasing levels of viruses associated with varroa or other pathologies of relevance to beekeeping production.

This point is interesting because different conclusions could be reached depending on the level of analysis: if only a few hives are evaluated in small areas the cause of death might be assigned to diseases or poor nutrition (derived from poor management by the beekeeper or deficiencies of the apiary site), but a higher level of analysis could possibly position agricultural intensification as the leading cause of decline in the floral offer and thus inadequate nutrition for the bees. In time, this would result in more severe immune suppression, which can be aggravated by different stressors, among which pesticides might play an important role (Nazzi & Pennacchio, 2014). This could turn out a negative spiral of harmful interactions, and the way out of it probably requires, at the very least, a territorial-level approach.

## Specific considerations regarding glyphosate

Since 2014, glyphosate has been used in more than 140 countries (Benbrook, 2016) and can be found in more than 750 formulated products (Guyton *et al*., 2015). Currently, it is the most widely used herbicide worldwide, as well as the most “politicized” agrochemical (Ledoux *et al*., 2020).

Strictly speaking, glyphosate is not directly applied to hives, but can be found around places where bees live, visit and forage (Berg *et al*., 2018). Since beekeeping and agricultural activities usually occur simultaneously and in the same territory, glyphosate can be easily transported to hives and pollute the supply of honey (Karise *et al*., 2017). There are numerous scientific studies reporting that bees can be exposed to glyphosate through pollen, nectar, and water during the search for food (Herbert *et al*., 2014; Karise *et al*., 2017; Goñalons & Farina, 2018). This pesticide can even enter the hives attached to the body of bees (Rortais *et al*., 2017) and consequently transfer this pollutant into the hive and its products (Dai *et al*., 2018). When glyphosate eventually enters the hive, it negatively affects learning behavior, an essential mechanism used during food gathering flights, in adult bees exposed to this herbicide (Herbert *et al*., 2014; Balbuena *et al*., 2015). However, clearly documented cases do not abound in the scientific literature due to the difficulties of collecting samples of stray bees and identifying the specific chemicals that cause the losses and at the same time ruling out other possible causes of the phenomenon.

## Potential impact dampeners to agricultural intensification and the use of pesticides

A number of researchers have suggested offering economic incentives to farmers to restore pollinator-friendly habitats, including the supply of flowers in or around fields and the elimination of insecticide use by adopting agroecological production methods (Nicholls *et al*., 2013; Prado *et al*., 2018). Some of these proposals were put into practice with encouraging results, albeit in reduced areas (Schulte *et al*., 2017; Kordbacheh *et al*., 2020). Nevertheless, for these strategies to have an effect and without forgetting the multi-causal nature of the problem, it is necessary that the proposed habitat restoration be, at least, on a regional scale.

The phenomenon of chemical contamination of bees and their products is supra-national in nature and therefore the palliative possibilities of the same scale should be considered, since there is little value in the efforts of individual beekeepers or farmers or grouped into small consortia in the face of the real size of the problem.

As previously mentioned, the possibility of chemical contamination of bees in agricultural landscapes is high. In fact, agricultural activities are decidedly the most common cause of loss of pollinators and/or contamination of their products for some authors (Potts *et al*., 2010b). Thus, it is appropriate to focus the analysis on the emerging environmental impact of soybean, one of the main crops, at least in terms of occupied area (particularly in the Americas) and its superlative economic relevance worldwide.

Extensive agriculture, widely represented in American continent by maize (*Zea mays*) and soybean (*Glycine max*), has grown to unprecedented levels in recent years (Hartman *et al*., 2011). This expansion of the sown area has been even proportionally larger for soybean in countries such as Argentina (Reboratti, 2010), Brazil and the USA (Pagano & Miransari, 2016). This has led to a loss of biodiversity at the landscape-level (Aizen, 2009) and habitat fragmentation (Pacheco, 2012) in large regions of the world. The soybeans crop is strongly linked to bio-technological developments that facilitate its production and allow to increasingly expand, the edaphoclimatic borders that make it possible to sow it.

The flight radius of *A. mellifera* is considerably extensive. Hagler *et al*. (2011) determined that honey bees have flight distances of up to 6 km; consequently, the foraging area of a hive or apiary is very significant (more than 11,000 ha). This area would cover numerous private farms anywhere in the world, even in countries with large areas of countryside such as Argentina, in which agricultural establishments in the Pampean region average between 200 and 500 ha (CNA, 2018). This fact, together with the need for approaches at the landscape-level mentioned above, highlights the need to promote large-scale actions, not action limited to a few farmers or in small areas. It is clear then that economic incentive strategies require very large sums of money and active policies historically delegated to the private sector.

Regardless of the multiple economic benefits this crop generates to farmers, it is clear that the continuous increase in area allocated to soybean and other crops (under the technique of hegemonic production, strongly dependent on agricultural inputs) affects the survival of bee colonies (both *Apis* and non-*Apis*), in two main ways:

**1) By the loss of the local flora available:** a multiplicity of fanerogamous species available for the foraging by honey bees provide diversity in the source of nectar and pollen, which is relevant for a successful immune response (Negri *et al*., 2015). Consequently, its deficiency (monocultures) is the cause of immune problems of various kinds in bees, especially in *A. mellifera* (Alaux *et al*., 2010; Castelli *et al*., 2020).

Although soybean flowering is relatively attractive to bees (Fagúndez *et al*., 2016b) and floral input is massive (millions of flowers/ha), this offering is only available in synchronous periods lasting for only a few weeks a year. This is also true for all extensive agricultural monocultures, which provide limited value forage resources for bees due to rapid growth with short periods of rotation and low floral diversity (Allsopp & Cherry, 2004; De Lange *et al*., 2013). Therefore, it has been proposed that chemical fallows (highly efficient in weed control) could be dispensed with and make use of old agricultural practices (use of plow), of massive use prior to the adoption of the direct sowinmethod (Altieri & Whitcomb, 1979), for soil preparation in agricultural areas, that improve the abundance and diversity of beneficial insects, including pollinators.

This simple proposal seemingly delivers promising, low-cost results. However, these practices are currently marginal, given the many agronomic disadvantages they entail (soil erosion, volatilization and carbon loss, subsurface soil compaction, etc), which have converged on the mass adoption of the direct seeding method with chemical fallows by most farmers (García *et al*., 2000). In fact, it is possible to ensure that there is a great dependence on chemical weed control of major extensive crops, even though mechanical weed control practices remain (Scursoni *et al*., 2019). In fact, the excellent control of weeds that pesticides allow explain much of the formidable agricultural success that reports yields that were unthinkable only a few decades ago. Thus, reverting to old agricultural practices would only be possible by increasing the area allocated to crops to support of current agricultural production, which in turn would entail even more environmental deterioration.

In line with this, the maintenance and restoration of hedges and other vegetation at the edges of the agricultural fields have been proposed to house pollinators (Garibaldi *et al*., 2013). Unfortunately, further work has determined that weeds and other plants on the edges of the fields are suppliers of pollen and nectar (often contaminated) to bees, by behaving as depositors of pesticides applied to adjacent crops and also other pesticides (frequently used to control nuisance pests such as mosquitoes) that were not applied to the crops (Long & Krupke, 2016). Fortunately, under certain conditions, pesticides on surrounding plants are observed in low concentrations (Hall *et al*., 2022).

**2) By the use of pesticides** (associated with crop safekeeping), which involves the weakening or death of bees (Malaspina *et al*., 2008).

The massive use of agricultural pesticides leads to the contamination of bees and their products (Pareja *et al*., 2011; Benuszak, 2017; Tosi *et al*., 2018). In an interesting review, Maggi *et al*. (2016) refer to numerous authors who blame pesticides for the loss of bees in agricultural areas of South America. For example, fipronil and imidacloprid have been detected in high doses in colonies of depopulated honey bees in Uruguay (Pareja *et al*., 2011). Additionally, pesticides can also affect non-*Apis* bee populations, as the harmful impact of insecticides on stingless bees has been documented (Barbosa *et al*., 2015).

At this point, most actions traditionally proposed to reduce pesticide damage to bees are aimed at counteracting the effect of nearby disturbances in time and space, for example, the proposal of transient closure of bottom boards in the face of imminent agricultural spraying near hives, the use of surfactants that reduce product drift or the restriction of sprays when the wind direction is towards the hive, among others (May *et al*., 2015).

It is tempting then to suggest mitigation strategies focused on to avoid pesticide drift and that spray at times when the bees do not exhibit foraging activity (Blettler *et al*., 2016). Unfortunately, this proposal might be too simplistic as well, if it is not accompanied by other strategies that converge on the same objective. It has recently been reported that bees make use of the floral resource of agricultural crops even if it has recently been sprayed with pesticides (Fagúndez *et al*., 2016a), which means that the most commonly used pesticide products for the control of agricultural pests do not present repellence, immediate or delayed, towards bees. This fact was proven in research conducted precisely on soybean crops, which indicates that the problem takes on another dimension and exposes the limitations of the previously proposed strategy since, according to these results (Fagúndez *et al*., 2016a), the problem would not be solved by keeping the bees away during sprays. On the contrary, it seems clear that it is the bees themselves that go voluntarily towards sprayed cultivation.

The behavior of foraging on recently pulverized soybean flowers acquires greater dimension considering that a positive effect of entomophilous pollination (promoted by *A. mellifera*) on the granary yields of soybeans has been proven (first in Brazil by Chiari *et al*., 2005 and later in Argentina by Blettler *et al*., 2018 and Garibaldi *et al*., 2021). Taking these findings into consideration, the incentive to provide pollination services to this crop to maximize the yields of this crop should be clear. Nevertheless, this has limited chances of effective application since the production technology of this crop currently demands huge amounts of pesticides for its protection of phytophagous insects (considering the width of the occupied area: soybeans cover 129 million hectares globally http://www.fao.org/faostat/en/#home), which limits the possibilities of a joint strategy involving managed and non-*Apis* bees pollinating insects.

Considering that 35% of the world's production comes from crops that depend on animal pollination (Gallai *et al*., 2009) and that honey bees are the main pollinating insect of these crops (Klein *et al*., 2007), it is crucial to understand that this problem no longer belongs to farmers or beekeepers alone, but to the society as a whole. Furthermore, in this work we challenge the widespread idea that the sum of partial solutions over a considerable period will lead to a substantive improvement in the problem since *it is essential to fully assess the consequences of interventions from a holistic perspective*.

## The problem with agonisms

A number of studies have identified negative effects of pesticides on bees even at very low concentrations (*i.e*., sublethalif considered individually) these adverse effects are magnified when certain combinations of pesticides are involved (Spurgeon *et al*., 2016), which is clear evidence of synergies between different products, even if the detected concentrations of these products are well below the concentrations of environmental relevance granted for each product individually (EFSA-PPR, 2012; Johnson, 2015; Rortais *et al*., 2017).

Unfortunately, even these relatively low concentrations cause synergistic or subletal effects on bee colonies such as decreased ability to survive the winter and decreased work of worker bees, alterations in foraging capacity, decreased pollen and honey reserves, irregularities in honeycomb construction, reduction in olfactory capacities, increase in the number of empty breeding cells, decrease in the production of queen bees, decrease in learning capacity and disorientation in the return flight to the hive (Liu *et al*., 2014). This becomes especially concerning if we consider that many of the commercial pesticides have a similar mode of action; consequently, the effects of additive toxicity on bees are very likely when bees and their larvae are exposed to a mixture of contaminants from the surrounding environment and/or from various treatments intended to preserve the health of the hives (Zhu *et al*., 2014).

Rortais *et al*. (2017) described examples of agonisms by similar action principles:

– Fungicides that inhibit ergosterol biosynthesis, in combination with neonicotinoids, pyrethroids and organophosphates.

– Acaricides such as coumaphos and fluvalinate in combination with antibiotics in the hive (oxytetracycline).

– Neonicotinoid insecticides in combination with antibiotics in the hive (oxytetracycline).

Additionally, other factors, such as poor bee nutrition, can exacerbate such mixing effects (Johnson *et al*., 2012). Taken together, all these factors result in a pressing need for more research on the underlying mechanisms of the synergistic effects of pesticides on the health of honey bees (Pettis *et al*., 2013).

## Risks to human health

So far, the problem of agricultural intensification and chemical contamination of hives has been addressed in relation to the impact on the survival and behaviour of bees and the negative effect on pollination of agricultural crops involved in the loss of pollinating services. However, an even more significant risk than those described above is faced by humans themselves, who are exposed to these chemical agents of known toxicity by consuming potentially contaminated bee products in their diet (Bommuraj *et al*., 2019). Importantly, the chemicals have the ability to bioaccumulate and biomagnify in the body over time (Al-Waili *et al*., 2012).

In each agronomic practice involving pesticides, it should be considered that honey bees that visited crop flowers or approached to sip water of guttation should be expected to come mostly from hives managed for food production, and they will be transporting contaminants that end up, sooner rather than later, as part of food products (Simon-Delso *et al*., 2017) and can cause commercialization problems for these products (Virgen, 2008). Although recent scientific literature suggests that exposure to pesticides through guttation water is unlikely to adversely affect honey bee colonies (Schmolke *et al*., 2018) this route cannot be particularly ruled out in places with little availability of clean water sources for bees (Böhme *et al*., 2017).

The two main products obtained from the hives are honey and pollen, and both are food for direct human consumption. Furthermore, they are subjected to very little treatment (pre-consumption) which is mostly reduced to minimum conditioning for commercial purposes and therefore the contaminants are not removed. In the face of this, the European Union establishes maximum permitted concentrations for certain products, which are called Maximum Residue Levels (MRLs). The MRL is the highest level of pesticide residue that is legally tolerated in or on food or feed when pesticides are applied correctly, to protect the general population and particularly vulnerable groups such as children and the unborn.

MRLs for honey are set in Regulation (EC) No. 396/2005 (OJ, 2005), and are calculated from data obtained from supervised field tests, performed under the critical use pattern detailed on labels of plant protection products. It is important to note that MRLs are not toxicological limits, but are toxicologically acceptable limits, under the assumption of an application that follows Good Agricultural Practices protocols, thus representing the maximum amount of waste that can be found in a plant-based food product because of the legal and rational use of phytosanitary products. In addition, it should be noted that standardized values have not been established globally, and unfortunately MRLs remain variable (Yamada, 2017). Additionally, developed countries likely have stricter regulations than developing countries, which often lack the resources and willingness to enforce pesticide residue legislation (Handford *et al*., 2015).

# A paradigm shift involving territorial management

To sum up, we will attempt to describe the problem of agricultural intensification and pesticide contamination in hives from a purely pragmatic approach. Given the immense use of pesticidesworldwidee, estimated at more than 6 million metric tons annually (Bernhardt *et al*., 2017), the growth of the area sown with soybeans, and the arrangement of hives in agricultural areas, shouldn't we expect even higher levels of pollution than those referenced? How is it possible that bees can live in such seemingly hostile environments? Clearly, there are factors that moderate the maximum theoretical damage, and it is crucial to understand these key factors to enhance them.

In this context, it is necessary to know with certainty what mechanisms operate, facilitate, or restrict the entry of pesticides into hives, because there is a possibility that pesticide access routes may not be as direct as is generally speculated. In some ways, bees appear to avoid the income of nectar or highly contaminated pollen, but at the same time, they cannot avoid the slow and gradual incomes of pesticides, particularly systemic in more residual doses, after days or even months after application (Ellis, 2010) or other likely income pathways not explored by the aforementioned works (application of pesticides for veterinary use, entry of pesticides via energy syrups, etc.). In this regard, Aizen *et al*. (2008) proposes that the impact of anthropic disturbances (agricultural spraying, for example) on the work of pollinators is not easily predictable a priori but is heavily contingent on the intensity of the disturbance and essentially depends on the spatial scale of the disturbance. Under this perspective, residue doses from past sprays throughout the bee exploration area would affect bee survival and product quality (honey and pollen) even more than immediate and nearby disturbances.

This possibility gains strength given the surprising mismatch between bee toxicity tests evaluated in the laboratory (controlled conditions) and in the field (several variables at play) (Barascou *et al*., 2021). That is, indirect exposures present significant problems, and this is relevant given the increase in the toxicity burden of pesticides in agricultural environments in recent years (Dibartolomeis *et al*., 2019).

If this were the case, agricultural regions could only guarantee pesticide-free beekeeping products prior to a period of quarantine necessary to detoxify the bee environment, even when habitat management strategy involving repopulations of native plant species or extreme care for health applications in the flowering period of crops were implemented. This quarantine period (whose duration could be extended to months or even years depending on the rate of degradation of the products present in the ecosystems) could be accurately evaluated by using bees as biosensors (De Oliveira *et al*., 2016). In this regard, the solutions cannot remain focused only on punitive actions towards those who avoid basic restrictions, such as: spraying with wind or with flowering crops or in the vicinity of apiaries, because these actions only challenge specific transgressions, whereas it seems that the problem of chemical contamination of bees and their products responds more to a slow and gradual accumulation of stressors that operate over time in certain landscapes than to a limited set of reprehensible actions.

For this reason, we consider that the real solution to these issues inescapably demands for territorial management. States, intermediate organizations with the predominant participation of researchers and experts, should develop strategies aimed at amalgamating economic productive interests with the protection of pollinator populations and the healthiness of beekeeping products. For example, by encouraging more traditionally managed farms (with certain logical restrictions on the use of pesticides but still guaranteeing good harvests as shown by some works that promote the biological regulation of pests (Gómez-Marco *et al*., 2016; de Pedro *et al*., 2021) where these farmers develop mostly extensive crops (soybean, corn, sorghum, wheat, etc.) that usually guarantee profitability to the sector and genuine economic income to the country. These farmers shall simultaneously ensure adequate rotations, applying erosion control and efficient water use practices. Under the proposed scheme, these farms should neighbour other farms with a more organic work profile that includes biological or environmental controllers instead of pesticides, prioritizing virgin or naturalized areas as well as production diversity that promotes nesting sites of native

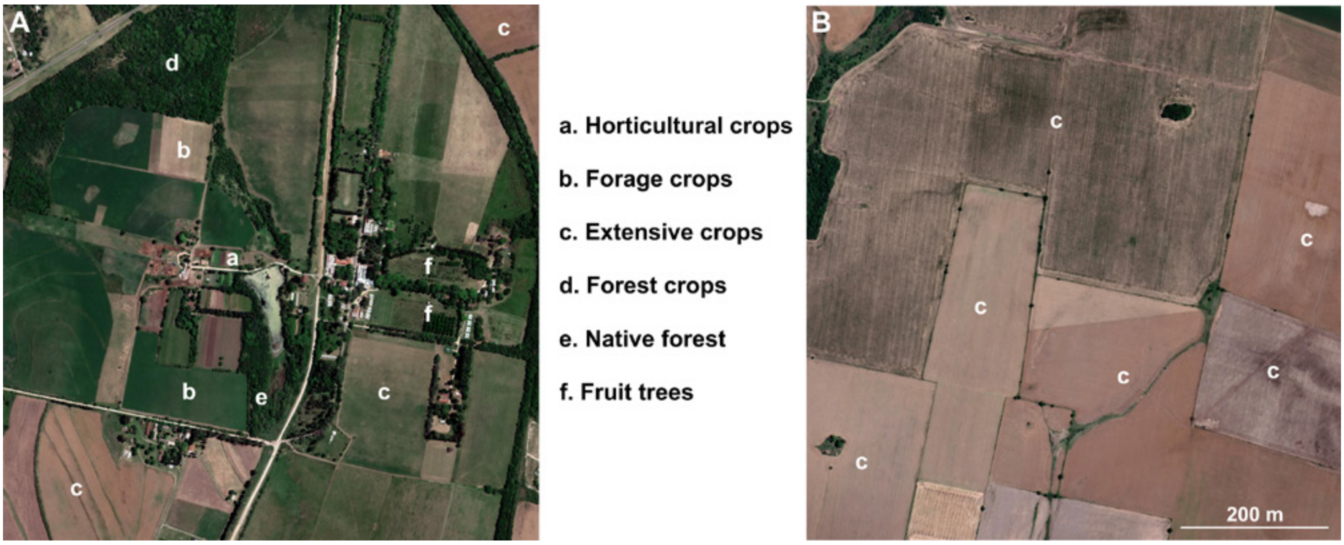


**Figure 3**. Examples of territorial management. Satellite images are 5 km apart, in an agroproductive region of Entre Ríos (Argentina). A) Honey bee-friendly environment, with agroecological diversity that does not compromise productivity. B) Parcels for extensive agriculture exclusively, that does not offer shelter or nutritional sources for bees. Map data ©2020 Maxar Technologies.

bees. Furthermore, a neighbouring livestock farm should be encouraged to sow different species (lucerne, *Lotus, Vicia*, etc.), which would ensure sporadic flowering patches and better distribution over time, thus offering a continuous source of flowers during the spring and summer seasons. Finally, it will also be necessary to ensure forest producers in neighbouring farms implement forest mountains that simultaneously conform barriers for wind protection, nesting seats and floral offers to ensure the survival of non-*Apis* pollinators and managed bees (Fig. 3).

With this proposed scheme, each of the actors at stake (traditional farmers, organic farmers, livestock, forestry, horticultural and fruit producers, etc.) would carry out the management of their farms without major impositions or restrictions. Furthermore, they would do so without further forecasting or care for pollinators, but the effects on the interconnected ecosystem would be seen only at levels of analysis that exceed private farms. Following this proposal, all the elements that the different researchers have deemed positive for the life of bees would be available at the landscape level. The proposed order should also keep in mind that diversity at the landscape level will be maximized with smaller farms, while ensuring minimum dimensions that ensure profitability.

## Authors' contributions

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## References

Agrebi EN, Tosi S, Wilmart O, Scippo ML, de Graaf DC, Saegerman C, 2020. Honey bee and consumer's exposure and risk characterisation to glyphosate-based herbicide (GBH) and its degradation product (AMPA): Residues in beebread, wax, and honey. Sci Total Environ 704: 135312. https://doi.org/10.1016/j.scitotenv.2019.135312

Aizen MA, Harder LD, 2009. The global stock of domesticated honey bees is growing slower than agricultural demand for pollination. Curr Biol 19(11): 915-918. https://doi.org/10.1016/j.cub.2009.03.071

Aizen MA, Garibaldi LA, Cunningham SA, Klein AM, 2008. Long-term global trends in crop yield and production reveal no current pollination shortage but increasing pollinator dependency. Curr Biol 18(20): 1572-1575. https://doi.org/10.1016/j.cub.2008.08.066

Aizen MA, Garibaldi LA, Dondo Bühler MB, 2009. Expansión de la soja y diversidad de la agricultura argentina. Ecología Austral 19(1): 45-54.

Alaux C, Ducloz F, Crauser D, Le Conte Y, 2010. Diet effects on honey bee immunocompetence. Biol Lett 6(4): 562-565. https://doi.org/10.1098/rsbl.2009.0986
Al-Waili N, Salom K, Al-Ghamdi A, Ansari MJ, 2012. Antibiotic, pesticide, and microbial contaminants of honey: human health hazards. The Sci World J 2012: 930849. https://doi.org/10.1100/2012/930849
Allsopp MH, Cherry M, 2004. An assessment of the impact on the bee and agricultural industries in the Western Cape of the clearing of certain Eucalyptus species using questionnaire survey data. Internal Final Report, 58. Nat Gov Rep South Africa, Dept Water Affairs, Pretoria (South Africa).
Altieri MA, Whitcomb WH, 1979. The potential use of weeds in the manipulation of beneficial insects agents in natural crop pest control. Hort Science 14(1): 12-18. https://doi.org/10.21273/HORTSCI.14.1.12
Amulen DR, Spanoghe P, Houbraken M, Tamale A, de Graaf DC, Cross P, Smagghe G, 2017. Environmental contaminants of honey bee products in Uganda detected using LC-MS/MS and GC-ECD. PLoS ONE 12(6): e0178546. https://doi.org/10.1371/journal.pone.0178546
Antonini C, Argilés-Bosch JM, 2017. Productivity and environmental costs from intensification of farming. A panel data analysis across EU regions. J Clean Prod 140: 796-803. https://doi.org/10.1016/j.jclepro.2016.04.009
Arena M, Sgolastra F, 2014. A meta-analysis comparing the sensitivity of bees to pesticides. Ecotoxicol 23(3): 324-334. https://doi.org/10.1007/s10646-014-1190-1
Atwood D, Paisley-Jones C, 2017. Pesticides industry sales and usage: 2008-2012 market estimates. US Environmental Protection Agency, Washington, DC, 20460, 2017-01. https://www.epa.gov/pesticides/pesticides-industry-sales-and-usage-2008-2012-market-estimates [4th Dec 2020].
Azpiazu C, Bosch J, Bortolotti L, Medrzycki P, Teper D, Molowny-Horas R, *et al*, 2021. Toxicity of the insecticide sulfoxaflor alone and in combination with the fungicide fluxapyroxad in three bee species. Sci Rep 11(1): 1-9. https://doi.org/10.1038/s41598-021-86036-1
Balbuena MS, Tison L, Hahn ML, Greggers U, Menzel R, Farina WM, 2015. Effects of sublethal doses of glyphosate on honey bee navigation. J Exp Biol 218: 2799-2805. https://doi.org/10.1242/jeb.117291
Barascou L, Brunet JL, Belzunces L, Decourtye A, Henry M, Fourrier J, *et al*., 2021. Pesticide risk assessment in honeybees: Toward the use of behavioral and reproductive performances as assessment endpoints. Chemosphere 276: 130134. https://doi.org/10.1016/j.chemosphere.2021.130134
Barbosa WF, Smagghe G, Guedes RN, 2015. Pesticides and reduced-risk insecticides, native bees and pantropical stingless bees: Pitfalls and perspectives. Pest Manag Sci 71(8): 1049-1053. https://doi.org/10.1002/ps.4025
Belsky J, Joshi NK, 2019. Impact of biotic and abiotic stressors on managed and feral bees. Insects 10(8): 233. https://doi.org/10.3390/insects10080233
Benbrook CM, 2016. Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur 28(1): 3. https://doi.org/10.1186/s12302-016-0070-0
Benuszak J, Laurent M, Chauzat M, 2017. The exposure of honey bees (*Apis mellifera;* Hymenoptera: Apidae) to pesticides: Room for improvement in research. Sci Total Environ 587: 423-438. https://doi.org/10.1016/j.scitotenv.2017.02.062
Berg CJ, King HP, Delenstarr G, Kumar R, Rubio F, Glaze T, 2018. Glyphosate residue concentrations in honey attributed through geospatial analysis to proximity of large-scale agriculture and transfer off-site by bees. PLoS One 13(7): e0198876. https://doi.org/10.1371/journal.pone.0198876
Bernardi S, Venturino E, 2016. Viral epidemiology of the adult *Apis mellifera* infested by the *Varroa destructor* mite. Heliyon 2(5): e00101. https://doi.org/10.1016/j.heliyon.2016.e00101
Bernhardt ES, Rosi EJ, Gessner MO, 2017. Synthetic chemicals as agents of global change. Front Ecol Environ 15(2): 84-90. https://doi.org/10.1002/fee.1450
Biesmeijer JC, Roberts SP, Reemer M, Ohlemuller R, Edwards M, 2006. Parallel declines in pollinators and insect-pollinated plants in Britain and the Netherlands. Science 313: 351-354. https://doi.org/10.1126/science.1127863
Blettler D, Fagúndez G, Chémez MD, 2016. A study of the foraging schedule of honey bees on soy crops as an agronomical tool to mitigate the effects of agrochemicals. Scientia Interfluvius 7(2): 14-28.
Blettler DC, Fagúndez GA, Caviglia OP, 2018. Contribution of honey bees to soybean yield. Apidologie 49: 101-111. https://doi.org/10.1007/s13592-017-0532-4
Bommuraj V, Chen Y, Klein H, Sperling R, Barel S, Shimshoni JA, 2019. Pesticide and trace element residues in honey and beeswax combs from Israel in association with human risk assessment and honey adulteration. Food Chem 299: 125123. https://doi.org/10.1016/j.foodchem.2019.125123
Böhme F, Bischoff G, Zebitz CP, Rosenkranz P, Wallner K, 2017. Chronic exposure of honey bees, *Apis mellifera* (Hymenoptera: Apidae), to a pesticide mixture in realistic field exposure rates. Apidologie 48(3): 353-363. https://doi.org/10.1007/s13592-016-0479-x
Brook BW, Sodhi NS, Bradshaw CJ, 2008. Synergies among extinction drivers under global change. Trends Ecol Evol 23: 453-460. https://doi.org/10.1016/j.tree.2008.03.011
Castelli L, Branchiccela B, Garrido M, Invernizzi C, Porrini M, Romero H, *et al*., 2020. Impact of nutritional stress on honey bee gut microbiota, immunity, and

*Nosema ceranae* infection. Microb Ecol 80(4): 908-919. https://doi.org/10.1007/s00248-020-01538-1

Chauzat MP, Martel AC, Cougoule N, Porta P, Lachaize J, Zeggane S, *et al*., 2011. An assessment of honey bee colony matrices, *Apis mellifera* (Hymenoptera: Apidae) to monitor pesticide presence in continental France. Environ Toxicol Chem 30(1): 103-111. https://doi.org/10.1002/etc.361

Chen C, Liu Z, Luo Y, Xu Z, Wang S, Zhang X, *et al*, 2017. Managed honey bee colony losses of the Eastern honey bee (*Apis cerana*) in China (2011-2014). Apidologie 48(5): 692-702. https://doi.org/10.1007/s13592-017-0514-6

Chhabra A, Geist H, Houghton RA, Haberl H, Alves D, Rudel T, 2006. Multiple impacts of land-use/cover change. In: Land-use and land-cover change, pp: 71-116. Springer, Berlin, Heidelberg. https://doi.org/10.1007/3-540-32202-7_4

Chiari WC, Toledo VDA, Ruvolo-Takasusuki MCC, Attencia VM, Costa FM, Kotaka CS, *et al*., 2005. Floral biology and behavior of Africanized honey bees *Apis mellifera* in soybean (*Glycine max* L. Merril). Brazil Archiv Biol Technol 48(3): 367-378. https://doi.org/10.1590/S1516-89132005000300006

Claudianos C, Ranson H, Johnson RM, Biswas S, Schuler MA, Berenbaum MR, *et al*., 2006. A deficit of detoxification enzymes: pesticide sensitivity and environmental response in the honey bee. Insect Mol Biol 15(5): 615-636. https://doi.org/10.1111/j.1365-2583.2006.00672.x

CNA 2018. Censo Nacional Agropecuario. https://cna2018.indec.gob.ar/?_ga=2.12913204.226677820.1586445731-1130372488.1586445731 [March 2020].

Dai P, Jack CJ, Mortensen AN, Bloomquist JR, Ellis JD, 2018. The impacts of chlorothalonil and diflubenzuron on *Apis mellifera* L. larvae reared in vitro. Ecotoxicol Environ Saf 164: 283-288. https://doi.org/10.1016/j.ecoenv.2018.08.039

De Lange WJ, Veldtman R, Allsopp MH, 2013. Valuation of pollinator forage services provided by *Eucalyptus cladocalyx*. J Environ Manag 125: 12-18. https://doi.org/10.1016/j.jenvman.2013.03.027

De Oliveira RC, do Nascimento Queiroz SC, da Luz CFP, Porto RS, Rath S, 2016. Bee pollen as a bioindicator of environmental pesticide contamination. Chemosphere 163: 525-534. https://doi.org/10.1016/j.chemosphere.2016.08.022

De Pedro L, López-Gallego E, Pérez-Marcos M, Ramírez-Soria MJ, Sanchez JA, 2021. Native natural enemies in Mediterranean melon fields can provide levels of pest control similar to conventional pest management with broad-spectrum pesticides. Biol Control 164: 104778. https://doi.org/10.1016/j.biocontrol.2021.104778

Dibartolomeis M, Kegley S, Mineau P, Radford R, Klein K, 2019. An assessment of acute insecticide toxicity loading (AITL) of chemical pesticides used on agricultural land in the United States. PLoS One 14(8): e0220029. https://doi.org/10.1371/journal.pone.0220029

Di Pasquale G, Salignon M, Le Conte Y, Belzunces LP, Decourtye A, Kretzschmar A, *et al*., 2013. Influence of pollen nutrition on honey bee health: do pollen quality and diversity matter? PloS One 8(8): e72016. https://doi.org/10.1371/journal.pone.0072016

EFSA-PPR, 2012. Scientific Opinion on the science behind the development of a risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA J 10(5): 2668. https://doi.org/10.2903/j.efsa.2012.2668

Ellis M, 2010. Pesticides applied to crops and honey bee toxicity. CAP updates. https://bee-health.extension.org/pesticides-applied-to-crops-and-honey-bee-toxicity/

Fagúndez GA, Blettler D, Krumrick CG, Bertos MA, Trujillo CG, 2016a. Do agrochemicals used during soybean flowering affect the visits of *Apis mellifera* L.? Span J Agric Res 14(1): e0301. https://doi.org/10.5424/sjar/2016141-7492

Fagundez GA, Reinoso PD, Aceñolaza PG, 2016b. Caracterización y fenología de especies de interés apícola en el departamento Diamante (Entre Ríos, Argentina). Bol Soc Arg Bot 51(2): 243-267. https://doi.org/10.31055/1851.2372.v51.n2.14837

FAO-WHO, 1997. Codex maximum limits for pesticide residues. http://www.fao.org/waicent/faostat/Pest-Residue/pest-e.htm#E11E3

FAOSTAT, 2017. FAO statistical databases, Rome. http://www.fao.org/faostat/en/#data

Foley JA, DeFries R, Asner GP, Barford C, *et al*., 2005. Global consequences of land use. Science 309(5734): 570-574. https://doi.org/10.1126/science.1111772

Foley K, Fazio G, Jensen AB, Hughes WO, 2012. Nutritional limitation and resistance to opportunistic Aspergillus parasites in honey bee larvae. J Invert Pathol 111(1): 68-73. https://doi.org/10.1016/j.jip.2012.06.006

Gallacher M, Justo AM, 2016. Uso de TICs en el sector agropecuario con énfasis en el subsector apícola de Argentina, Uruguay, República Dominicana y Costa Rica. Conf. El sector apícola y sus avances-Las TIC's. INTA, Instituto de Economía, Buenos Aires.

Gallai N, Salles JM, Settele J, Vaissière BE, 2009. Economic valuation of the vulnerability of world agriculture confronted with pollinator decline. Ecol Econ 68(3): 810-821. https://doi.org/10.1016/j.ecolecon.2008.06.014

García FO, Ambroggio M, Trucco V, 2000. No-tillage in the Pampas of Argentina: A success story. Better Crops Int 14: 24-27.

García-Chao M, Agruña MJ, Calvete GF, Sakkas V, Llompart M, Dagnac T, 2010. Validation of an off line solid phase extraction liquid chromatography-tandem mass spectrometry method for the determination of systemic insecticide residues in honey and pollen samples collected in apiaries from NW Spain. Anal Chim Acta 672(1-2): 107-113. https://doi.org/10.1016/j.aca.2010.03.011

Garibaldi LA, Steffan-Dewenter I, Winfree R, Aizen MA, Bommarco R, Cunningham SA, *et al.*, 2013. Wild pollinators enhance fruit set of crops regardless of honey bee abundance. Science 339(6127): 1608-1611. https://doi.org/10.1126/science.1230200

Garibaldi LA, Schulte LA, Jordar DNN, Carella DSG, Kremen C, 2021. Time to integrate pollinator science into soybean production. Trends Ecol Evol 36(7): 573-575. https://doi.org/10.1016/j.tree.2021.03.013

Genersch E, Von Der Ohe W, Kaatz H, Schroeder A, Otten C, Büchler R, *et al.*, 2010. The German bee monitoring project: a long term study to understand periodically high winter losses of honey bee colonies. Apidologie 41(3): 332-352. https://doi.org/10.1051/apido/2010014

Gierer F, Vaughan S, Slater M, Thompson HM, Elmore JS, Girling RD, 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

Gleiciani Bürger PR, Campos MJ, 2014. Aspects of landscape and pollinators what is important to bee conservation? Diversity 6(1): 158-175. https://doi.org/10.3390/d6010158

Gómez-Marco F, Urbaneja A, Tena A, 2016. A sown grass cover enriched with wild forb plants improves the biological control of aphids in citrus. Basic Appl Ecol 17(3): 210-219. https://doi.org/10.1016/j.baae.2015.10.006

Goñalons CM, Farina WM, 2018. Impaired associative learning after chronic exposure to pesticides in young adult honey bees. J Exp Biol 221(7): jeb176644. https://doi.org/10.1242/jeb.176644

Goulson D, 2014. Pesticides linked to bird declines. Nature 511(7509): 295-296. https://doi.org/10.1038/nature13642

Goulson D, Nicholls E, Botías C, Rotheray EL, 2015. Bee declines driven by combined stress from parasites, pesticides, and lack of flowers. Science 347(6229). https://doi.org/10.1126/science.1255957

Grant MJ, Booth A, 2009. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Inform Libr J 26(2): 91-108. https://doi.org/10.1111/j.1471-1842.2009.00848.x

Guyton KZ, Loomis D, Grosse Y, El Ghissassi F, Benbrahim-Tallaa L, Guha N, *et al.*, 2015. International Agency for Research on Cancer Monograph Working Group ILF. Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. Lancet Oncology 16(5): 490-491. https://doi.org/10.1016/S1470-2045(15)70134-8

Hagler JR, Mueller S, Teuber LR, Machtley SA, Van Deynze A, 2011. Foraging range of honey bees, *Apis mellifera*, in alfalfa seed production fields. J Insect Sci 11(1): 144. https://doi.org/10.1673/031.011.14401

Hall MJ, Zhang G, O'Neal ME, Bradbury SP, Coats JR, 2022. Quantifying neonicotinoid insecticide residues in milkweed and other forbs sampled from prairie strips established in maize and soybean fields. Agr Ecosyst Environ 325: 107723. https://doi.org/10.1016/j.agee.2021.107723

Handford CE, Elliott CT, Campbell K, 2015. A review of the global pesticide legislation and the scale of challenge in reaching the global harmonization of food safety standards. Integr Environ Assess Manag 11(4): 525-536. https://doi.org/10.1002/ieam.1635

Hardstone MC, Scott JG, 2010. Is *Apis mellifera* more sensitive to insecticides than other insects? Pest Manag Sci 66(11): 1171-1180. https://doi.org/10.1002/ps.2001

Hartman GL, West ED, Herman TK, 2011. Crops that feed the World 2. Soybean - Worldwide production, use, and constraints caused by pathogens and pests. Food Secur 3(1): 5-17. https://doi.org/10.1007/s12571-010-0108-x

Herbert LT, Vázquez DE, Arena A, Farina WM, 2014. Effects of field-realistic doses of glyphosate on honey bee appetitive behaviour. J Exp Biol 217(19): 3457-3464. https://doi.org/10.1242/jeb.109520

Irungu J, Fombong AT, Kurgat J, Mulati P, Ongus J, Nkoba, *et al.*, 2016. Analysis of honey bee hive products as a model for monitoring pesticide usage in agroecosystems. J Environ Earth Sci 6(8): 2225-0948.

Johnson RM, 2015. Honey bee toxicology. Annu Rev Entomol 60: 415-434. https://doi.org/10.1146/annurev-ento-011613-162005

Johnson RM, Mao W, Pollock HS, Niu G, Schuler MA, Berenbaum MR, 2012. Ecologically appropriate xenobiotics induce cytochrome P450s in *Apis mellifera*. PLoS One 7(2): e31051. https://doi.org/10.1371/journal.pone.0031051

Karise R, Raimets R, Bartkevics V, Pugajeva I, Pihlik P, Keres I, *et al.*, 2017. Are pesticide residues in honey related to oilseed rape treatments? Chemosphere 188: 389-396. https://doi.org/10.1016/j.chemosphere.2017.09.013

Kiatoko N, Raina SK, Van Langevelde F, 2017. Impact of habitat degradation on species diversity and nest abundance of fve African stingless bee species in a tropical rainforest of Kenya. Int J Trop Insect Sci 37(3): 189-197. https://doi.org/10.1017/S174275841700011X

Klein AM, Vaissiere BE, Cane JH, Dewenter IS, Cunningham SA, Kremen C, *et al.*, 2007. Importance of pollinators in changing landscapes for world crops. Proc Roy Soc B: Biol Sci 274: 303-313. https://doi.org/10.1098/rspb.2006.3721

Klein Goldewijk K, Beusen A, Van Drecht G, De Vos M, 2011. The HYDE 3.1 spatially explicit database of human-induced global land-use change over the past 12,000 years. Glob Ecol Biogeogr 20(1): 73-86. https://doi.org/10.1111/j.1466-8238.2010.00587.x

Kordbacheh F, Liebman M, Harris M, 2020. Strips of prairie vegetation placed within row crops can sustain native bee communities. PloS One 15(10): e0240354. https://doi.org/10.1371/journal.pone.0240354

Kremen C, Williams NM, Thorp RW, 2002. Crop pollination from native bees at risk from agricultural intensification. P Nat Acad Sci USA 99: 16812-16816. https://doi.org/10.1073/pnas.262413599

Kulhanek K, Steinhauer N, Rennich K, Caron DM, Sagili RR, Pettis JS, *et al.*, 2017. A national survey of managed honey bee 2015-2016 annual colony losses in the USA. J Apic Res 56(4): 328-340. https://doi.org/10.1080/00218839.2017.1344496

Laio F, Ridolfi L, D'Odorico P, 2016. The past and future of food stocks. Environ Res Lett 11(3): 035010. https://doi.org/10.1088/1748-9326/11/3/035010

Ledoux ML, Hettiarachchy N, Yu X, Howard L, Lee SO, 2020. Penetration of glyphosate into the food supply and the incidental impact on the honey supply and bees. Food Control 109: 106859. https://doi.org/10.1016/j.foodcont.2019.106859

Liu J, Kuang W, Zhang Z, Xu X, Qin Y, Ning J, *et al.*, 2014. Spatiotemporal characteristics, patterns, and causes of land-use changes in China since the late 1980s. J Geograph Sci 24(2): 195-210. https://doi.org/10.1007/s11442-014-1082-6

Long EY, Krupke CH, 2016. Non-cultivated plants present a season-long route of pesticide exposure for honey bees. Nature Commun 7(1): 1-12. https://doi.org/10.1038/ncomms11629

Maggi M, Antúnez K, Invernizzi C, Aldea P, Vargas M, Negri P, *et al.*, 2016. Honey bee health in South America. Apidologie 47(6): 835-854. https://doi.org/10.1007/s13592-016-0445-7

Malaspina O, Souza TF, Zacarin ECMS, Cruz AS, Jesus D, 2008. Efeitos provocados por agrotóxicos em abelhas no Brasil. VIII Encontro Sobre Abelhas. Resumos. Ribeirão Preto: FUNPEC, 41-48.

Malhat FM, Haggag MN, Loutfy NM, Osman MA, Ahmed MT, 2015. Residues of organochlorine and synthetic pyrethroid pesticides in honey, an indicator of ambient environment, a pilot study. Chemosphere 120: 457-461. https://doi.org/10.1016/j.chemosphere.2014.08.032

May E, Wilson J, Isaacs R, 2015. Minimizing pesticide risk to bees in fruit crops. Extens Bull Michigan Stat Univ-E3245, 1-16.

Medici SK, Blando M, Sarlo E, Maggi M, Espinosa JP, Ruffinengo S, *et al.*, 2019. Pesticide residues used for pest control in honey bee colonies located in agroindustrial areas of Argentina. Int J Pest Manag 66(2): 163-172. https://doi.org/10.1080/09670874.2019.1597996

Mitchell EA, Mulhauser B, Mulot M, Mutabazi A, Glauser G, Aebi A, 2017. A worldwide survey of neonicotinoids in honey. Science 358(6359): 109-111. https://doi.org/10.1126/science.aan3684

Muli E, Kilonzo J, Dogley N, Monthy G, Kurgat J, Irungu J, *et al.*, 2018. Detection of pesticide residues in selected bee products of honey bees (*Apis mellifera* L.) colonies in a preliminary study from Seychelles archipelago. Bull Environ Contam Toxicol 101(4): 451-457. https://doi.org/10.1007/s00128-018-2423-4

Mullin CA, Frazier M, Frazier JL, Ashcraft S, Simonds R, VanEngelsdorp D, *et al.*, 2010. High levels of miticides and agrochemicals in North American apiaries: implications for honey bee health. PLoS One 5(3): e9754. https://doi.org/10.1371/journal.pone.0009754

Nazzi F, Pennacchio F, 2014. Disentangling multiple interactions in the hive ecosystem. Trends Parasitol 30(12): 556-561. https://doi.org/10.1016/j.pt.2014.09.006

Negri P, Maggi MD, Ramirez L, De Feudis L, Szwarski N, Quintana S, *et al.*, 2015. Abscisic acid enhances the immune response in *Apis mellifera* and contributes to the colony fitness. Apidologie 46(4): 542-557. https://doi.org/10.1007/s13592-014-0345-7

Nicholls CI, Altieri MA, 2013. Plant biodiversity enhances bees and other insect pollinators in agroecosystems. A review. Agron Sustain Dev 33(2): 257-274. https://doi.org/10.1007/s13593-012-0092-y

OJ, 2005. Regulation (EC) nº 396/2005 of the European Parliament and of the Council on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. http://data.europa.eu/eli/reg/2005/396/oj

Olate-Olave VR, Verde M, Vallejos L, Perez Raymonda L, Cortese MC, Doorn M, 2021. Bee health and productivity in *Apis mellifera*, a consequence of multiple factors. Vet Sci 8(5): 76. https://doi.org/10.3390/vetsci8050076

Pacheco P, 2012. Actor and frontier types in the Brazilian Amazon: Assessing interactions and outcomes associated with frontier expansion. Geoforum 43(4): 864-874. https://doi.org/10.1016/j.geoforum.2012.02.003

Pagano MC, Miransari M, 2016. The importance of soybean production worldwide. In: Abiotic and biotic stresses in soybean production, pp: 1-26. Academic Press. https://doi.org/10.1016/B978-0-12-801536-0.00001-3

Panseri S, Catalano A, Giorgi A, Arioli F, Procopio A, Britti D, *et al.*, 2014. Occurrence of pesticide residues in Italian honey from different areas in relation to its potential contamination sources. Food Control 38: 150-156. https://doi.org/10.1016/j.foodcont.2013.10.024

Pareja L, Colazzo M, Pérez-Parada A, Niell S, Carrasco-Letelier L, Besil N, *et al.*, 2011. Detection of pesticides in active and depopulated beehives in Uruguay. Int J Environ Res Public Health 8(10): 3844-3858. https://doi.org/10.3390/ijerph8103844

Pettis JS, Lichtenberg EM, Andree M, Stitzinger J, Rose R, 2013. Crop pollination exposes honey bees to pesticides which alters their susceptibility to the gut pathogen Nosema ceranae. PLoS One 8(7): e70182. https://doi.org/10.1371/journal.pone.0070182

Pirk CW, Human H, Crewe RM, VanEngelsdorp D, 2014. A survey of managed honey bee colony losses in the Republic of South Africa-2009 to 2011. J Apic Res 53(1): 35-42. https://doi.org/10.3896/IBRA.1.53.1.03

Powney GD, Carvell C, Edwards M, Morris RK, Roy HE, Woodcock BA, *et al.*, 2019. Widespread losses of pollinating insects in Britain. Nature Commun 10(1): 1-6. https://doi.org/10.1038/s41467-019-08974-9

Population Reference Bureau, 2017. World Population Data Sheet (2017) Washington, DC. https://www.prb.org/international/indicator/population/snapshot/, [8th Dec 2020].

Potts SG, Biesmeijer JC, Kremen C, Neumann P, Schweiger O, Kunin WE, 2010a. Global pollinator declines: trends, impacts and drivers. Trends Ecol Evol 25(6): 345-353. https://doi.org/10.1016/j.tree.2010.01.007

Potts SG, Roberts SP, Dean R, Marris G, Brown MA, Jones R, *et al.*, 2010b. Declines of managed honey bees and beekeepers in Europe. J Apic Res 49(1): 15-22. https://doi.org/10.3896/IBRA.1.49.1.02

Prado MM, García DG, Sastre RM, 2018. Los insectos polinizadores en la agricultura: importancia y gestión de su biodiversidad. Ecosistemas 27(2): 81-90. https://doi.org/10.7818/ECOS.1394

Ramankutty N, Foley JA, 1999. Estimating historical changes in global land cover: Croplands from 1700 to 1992. Glob Biogeochem Cycl 13(4): 997-1027. https://doi.org/10.1029/1999GB900046

Rapisarda VM, Hussein AM, 2002. Nuclear technology and beekeeping industry: much more than atoms and bees. Rev Comis Nac Energ Atom 2(5/6): 5-11.

Ravoet J, Reybroeck W, de Graaf DC, 2015. Pesticides for apicultural and/or agricultural application found in Belgian honey bee wax combs. Bull Environ Contam Toxicol 94(5): 543-548. https://doi.org/10.1007/s00128-015-1511-y

Reboratti C, 2010. Un mar de soja: la nueva agricultura en Argentina y sus consecuencias. Rev Geograf Norte Grande (45): 63-76. https://doi.org/10.4067/S0718-34022010000100005

Rortais A, Arnold G, Dorne JL, More SJ, Sperandio G, Streissl F, *et al.*, 2017. Risk assessment of pesticides and other stressors in bees: principles, data gaps and perspectives from the European Food Safety Authority. Sci Total Environ 587: 524-537. https://doi.org/10.1016/j.scitotenv.2016.09.127

Sánchez-Bayo F, Wyckhuys KA, 2019. Worldwide decline of the entomofauna: A review of its drivers. Biol Conserv 232: 8-27. https://doi.org/10.1016/j.biocon.2019.01.020

Schmolke A, Kearns B, O'Neill B, 2018. Plant guttation water as a potential route for pesticide exposure in honey bees: a review of recent literature. Apidologie 49(5): 637-646. https://doi.org/10.1007/s13592-018-0591-1

Schulte LA, Niemi J, Helmers MJ, Liebman M, Arbuckle JG, James DE, *et al.*, 2017. Prairie strips improve biodiversity and the delivery of multiple ecosystem services from corn-soybean croplands. P Nat Acad Sci 114(42): 11247-11252. https://doi.org/10.1073/pnas.1620229114

Scursoni JA, Vera ACD, Oreja FH, Kruk BC, de la Fuente EB, 2019. Weed management practices in Argentina crops. Weed Technol 33(3): 459-463. https://doi.org/10.1017/wet.2019.26

Seto KC, Güneralp B, Hutyra LR, 2012. Global forecasts of urban expansion to 2030 and direct impacts on biodiversity and carbon pools. P Nat Acad Sci 109(40): 16083-16088. https://doi.org/10.1073/pnas.1211658109

Sgolastra F, Blasioli S, Renzi T, Tosi S, Medrzycki P, Molowny-Horas R, *et al.*, 2018. Lethal effects of Cr (III) alone and in combination with propiconazole and clothianidin in honey bees. Chemosphere 191: 365-372. https://doi.org/10.1016/j.chemosphere.2017.10.068

Simon-Delso N, San Martin G, Bruneau E, Delcourt C, Hautier L, 2017. The challenges of predicting pesticide exposure of honey bees at landscape level. Sci Rep 7(1): 1-10. https://doi.org/10.1038/s41598-017-03467-5

Spurgeon D, Hesketh H, Lahive E, Svendsen C, Baas J, Robinson A, *et al.*, 2016. Chronic oral lethal and sub-lethal toxicities of different binary mixtures of pesticides and contaminants in bees (*Apis mellifera*, *Osmia bicornis* and *Bombus terrestris*). EFSA Supp Publ 13(9). https://doi.org/10.2903/sp.efsa.2016.EN-1076

Steinhauer N, Kulhanek K, Antúnez K, Human H, Chantawannakul P, Chauzat MP, 2018. Drivers of colony losses. Curr Opin Insect Sci 26: 142-148. https://doi.org/10.1016/j.cois.2018.02.004

Tosi S, Costa C, Vesco U, Quaglia G, Guido G, 2018. A 3-year survey of Italian honey bee-collected pollen reveals widespread contamination by agricultural pesticides. Sci Total Environ 615: 208-218. https://doi.org/10.1016/j.scitotenv.2017.09.226

UN FAO, 2017. Driving action across the 2030 agenda for sustainable development/ sustainable development goals/ food and agriculture organization of the United Nations.

Valdovinos-Flores C, Alcantar-Rosales VM, Gaspar-Ramírez O, Saldaña-Loza LM, Dorantes-Ugalde JA, 2017. Agricultural pesticide residues in honey and wax combs from Southeastern, Central and Northeastern Mexico. J Apic Res 56(5): 667-679. https://doi.org/10.1080/00218839.2017.1340798

Vandame R, Palacio MA, 2010. Preserved honey bee health in Latin America: a fragile equilibrium due to low-intensity agriculture and beekeeping? Apidologie 41(3): 243-255. https://doi.org/10.1051/apido/2010025

Van Eck NJ, Waltman L, 2014. CitNetExplorer: A new software tool for analyzing and visualizing citation networks. J Informetrics 8(4): 802-823. https://doi.org/10.1016/j.joi.2014.07.006

Van Engelsdorp D, Evans JD, Saegerman C, Mullin C, Haubruge E, Nguyen BK, *et al.*, 2009. Colony collapse disorder: a descriptive study. PloS One 4(8): e6481. https://doi.org/10.1371/journal.pone.0006481

Van Engelsdorp D, Traynor KS, Andree M, Lichtenberg EM, Chen Y, Saegerman C, *et al*., 2017. Colony collapse disorder (CCD) and bee age impact honey bee pathophysiology. PLoS One 12(7): e0179535. https://doi.org/10.1371/journal.pone.0179535

Vaudo AD, Tooker JF, Grozinger CM, Patch HM, 2015. Bee nutrition and floral resource restoration. Curr Opin Insect Sci 10: 133-141. https://doi.org/10.1016/j.cois.2015.05.008

Virgen MM, 2008. Estudio de la contaminación por pesticidas organoclorados, organofosforados y por bifernilos policlorados en miel producida en la Comunidad Autónoma de Aragón. Doctoral diss., Univ. Zaragoza, Spain.

Watson K, Stallins JA, 2016. Honey bees and colony collapse disorder: A pluralistic reframing. Geograph Compass 10(5): 222-236. https://doi.org/10.1111/gec3.12266

Winfree R, Bartomeus I, Cariveau DP, 2011. Native pollinators in anthropogenic habitats. Annu Rev Ecol Evol Syst 42: 1-22. https://doi.org/10.1146/annurev-ecolsys-102710-145042

Wu JY, Smart MD, Anelli CM, Sheppard WS, 2012. Honey bees (*Apis mellifera*) reared in brood combs containing high levels of pesticide residues exhibit increased susceptibility to Nosema (Microsporidia) infection. J Invert Pathol 109(3): 326-329. https://doi.org/10.1016/j.jip.2012.01.005

Yamada Y, 2017. Importance of Codex Maximum Residue Limits for pesticides for the health of consumers and international trade, Chapter 7. In: Food safety assessment of pesticide residues, pp. 269-282. World Scientific. https://doi.org/10.1142/9781786341693_0007

Zhang W, Jiang F, Ou J, 2011. Global pesticide consumption and pollution: with China as a focus. Proc Int Acad Ecol Environ Sci 1(2): 125.

Zhu W, Schmehl DR, Mullin CA, Frazier JL, 2014. Four common pesticides, their mixtures and a formulation solvent in the hive environment have high oral toxicity to honey bee larvae. PLoS One 9(1): e77547. https://doi.org/10.1371/journal.pone.0077547