Contents lists available at ScienceDirect



Review

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv



Pesticides and pollinators: A socioecological synthesis



Douglas B. Sponsler ^{a,*}, Christina M. Grozinger ^a, Claudia Hitaj ^b, Maj Rundlöf ^{c,d}, Cristina Botías ^e, Aimee Code ^f, Eric V. Lonsdorf ^g, Andony P. Melathopoulos ^h, David J. Smith ^b, Sainath Suryanarayanan ⁱ, Wayne E. Thogmartin ^j, Neal M. Williams ^d, Minghua Zhang ^k, Margaret R. Douglas ¹

^a Pennsylvania State University, Department of Entomology, Center for Pollinator Research, Huck Institutes of the Life Sciences, USA

^b U. S. Department of Agriculture, Economic Research Service, Washington, D.C., USA

^c Lund University, Department of Biology, 223 62 Lund, Sweden

^d University of California, Department of Entomology and Nematology, Davis, CA 95616, USA

e Laboratorio de Patología Apícola, Centro de Investigación Apícola y Agroambiental, IRIAF, Consejería de Agricultura de la Junta de Comunidades de Castilla-La Mancha, 19180 Marchamalo, Spain

f Xerces Society for Invertebrate Conservation, USA

^g University of Minnesota, Institute on the Environment, USA

^h Oregon State University, Department of Horticulture, USA

¹ University of Wisconsin-Madison, Population Health Institute, Nelson Institute for Environmental Studies, Madison, WI 53706, USA

^j U.S. Geological Survey, Upper Midwest Environmental Sciences Center, La Crosse, WI 54603, USA

k Department of Land, Air and Water Resources, University of California Davis, One Shields Ave, Davis, CA 95616, USA

¹ Dickinson College, Department of Environmental Studies & Environmental Science, Carlisle, PA 17013, USA

HIGHLIGHTS

GRAPHICAL ABSTRACT



· Pesticide-pollinator research has tended to be compartmentalized and intradisciplinary.

- The pesticide-pollinator system spans from upstream drivers to higher-order effects on populations and ecosystems.
- We present a framework consisting of three overlapping domains: pesticide use, pesticide exposure, and pesticide effects.
- Future scholarship would benefit from integration across these domains and the filling of gaps within them.

ARTICLE INFO

Article history: Received 24 August 2018 Received in revised form 1 January 2019 Accepted 3 January 2019 Available online 6 February 2019

Editor: Yolanda Picó

Keywords: Risk assessment Bee

Domain 1: Pesticide use	
Domain 1: Pesticide use	
Spatiotemporal patterns of polinator activity of contamination	
	_
Domain 2: Pesticide Exposure Toxicity	
Effects on polinators	
Domain 3: Pesticide Effects en coopstem functions and services	J

ABSTRACT

The relationship between pesticides and pollinators, while attracting no shortage of attention from scientists, regulators, and the public, has proven resistant to scientific synthesis and fractious in matters of policy and public opinion. This is in part because the issue has been approached in a compartmentalized and intradisciplinary way, such that evaluations of organismal pesticide effects remain largely disjoint from their upstream drivers and downstream consequences. Here, we present a socioecological framework designed to synthesize the pesticide-pollinator system and inform future scholarship and action. Our framework consists of three interlocking domains-pesticide use, pesticide exposure, and pesticide effects-each consisting of causally linked patterns, processes, and states. We elaborate each of these domains and their linkages, reviewing relevant literature and providing empirical case studies. We then propose guidelines for future pesticide-pollinator scholarship and action agenda aimed at strengthening knowledge in neglected domains and integrating knowledge

* Corresponding author at: Millennium Science Complex W-234A, University Park, PA 16802, USA. E-mail address: dbs31@psu.edu (D.B. Sponsler).

https://doi.org/10.1016/j.scitotenv.2019.01.016

0048-9697/© 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

across domains to provide decision support for stakeholders and policymakers. Specifically, we emphasize (1) stakeholder engagement, (2) mechanistic study of pesticide exposure, (3) understanding the propagation of pesticide effects across levels of organization, and (4) full-cost accounting of the externalities of pesticide use and regulation. Addressing these items will require transdisciplinary collaborations within and beyond the scientific community, including the expertise of farmers, agrochemical developers, and policymakers in an extended peer community.

© 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Contents

1.	Introduct	tion							
2.	Pesticide	use (Domain 1)							
	2.1. Pe	est pressure							
	2.2. Pe	esticide availability: Development and regulation							
	2.3. In	Iformation and values							
3.	Pesticide	exposure (Domain 2)							
	3.1. Pe	esticide use and environmental fate							
	3.2. Pc	ollinator behavior and life history							
	3.	2.1. General behavioral and life history traits							
	3.3. Pa	atterns of exposure							
4.	Pesticide	effects (Domain 3)							
	4.1. To	oxicity and effects on individual pollinators							
	4.2. Pr	ropagating effects to colonies, populations, and systems \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots 102°							
5.	Applicatio	on and conclusion							
	5.1. Pr	riority 1: Stakeholder engagement							
	5.2. Pr	riority 2: Mechanistic exposure modeling and descriptive natural history							
	5.3. Pr	riority 3: Mechanistic effects modeling and longitudinal monitoring							
	5.4. Pr	riority 4: Full-cost accounting							
	5.5. Pc	ollinators and pesticides in context							
Ack	nowledgme	ents							
References									

1. Introduction

Pollinators are animals that mediate the exchange of pollen between flowers, facilitating fruit and seed production in roughly 88% of flowering plants (Ollerton et al., 2011). While a broad range of animal taxa can function as pollinators (Ollerton, 2017), bees (Hymenoptera: Anthophila) are uniquely specialized for pollen transport and account for the bulk of pollination services in both wild and cultivated plants, complemented principally by other insect pollinators (Willmer et al., 2017). The manifold significance of pollinators–as providers of ecosystem services, keystones of natural systems, and models for theoretical study–and the seriousness of recent patterns of pollinator decline (Ollerton, 2017) are evident not only to the expert communities of ecology and agriculture but also the public at large.

The ubiquity with which pollinating insects interact with humandominated landscapes brings them into frequent intersection with anthropogenic chemicals. These include chemical pesticides designed specifically for deleterious action against plants, animals, or microbes deemed incompatible with human interests, particularly those that threaten agricultural yield or vector disease. In the case of insecticides there exists self-evident potential for off-target harm to pollinating insects, but even when insects are not the target-as in the case of fungicide and herbicide use-they may be directly or indirectly affected, both by the active and putatively inert (Mullin, 2015) ingredients of the pesticides they encounter (discussed in Section 4.1).

Instances of "bee kills" associated with pesticide use have been documented since the late 19th century (Berenbaum, 2016), but the discovery in the mid-2000s of parallel declines in wild pollinators and pollinator-dependent plants (Biesmeijer et al., 2006) along with widespread losses of managed honey bees (Neumann and Carreck, 2010) raised the possibility that the effects of pesticides on pollinators might be more than merely episodic. As the scientific literature on pesticidepollinator interaction grew rapidly to a burgeoning corpus of over 2000 publications, what emerged was not a systematic conclusion but a catalogue of complexities: combinatorial exposures (Mullin et al., 2010), interactions and synergisms (Johnson et al., 2013; Sánchez-Bayo et al., 2016), sublethal effects (Desneux et al., 2006), inter- and intra-specific variation in susceptibility (Arena and Sgolastra, 2014; Poquet et al., 2016), buffering mechanisms in social colonies (Henry et al., 2015), and unexpected routes of exposure (Krupke et al., 2012). Any frank synthesis of this literature must acknowledge that despite considerable insights at the scale of organismal toxicology, the upstream patterns and processes that govern the initial exposure of pollinators to pesticides remain obscure. Knowledge is similarly truncated in the downstream direction, with relatively few studies linking organismal effects to colony- or population-level outcomes, and even fewer to the system-level outcomes of biodiversity conservation, pollination services, and apicultural productivity that are the explicit protection goals of government regulatory agencies. These missing linkages currently hinder both theoretical synthesis of pesticide-pollinator science and its application to decision support for stakeholders and regulators, a problem that calls for transdisciplinary approaches to integrate the socioeconomic, toxicological, and ecological dimensions of the system.

Here, we present a conceptual framework designed to facilitate such integration. Our framework consists of three interlocking domains of causal relationships (Fig. 1). Domain 1 focuses on the human and ecological drivers governing pesticide use. The resulting spatiotemporal patterns of pesticide use comprise the input to Domain 2, where they interact with pesticide fate dynamics and pollinator behavior and life history to produce patterns of pollinator exposure. In Domain 3, patterns of exposure interact with pesticide toxicity to determine effects at the



Fig. 1. A conceptual framework of the pollinator-pesticide system. Domains of causal relationships overlap at key linking phenomena (yellow). The main direction of causation is indicated by arrows, generally flowing top-to-bottom, except for the potential feedback (dashed line) of Domain 3 to Domain 1.

individual, colony, population, and ecosystem levels. The feedback of Domain 3 effects on Domain 1 use patterns closes our framework into an iterable system in which pesticide use decisions can be informed and affected by pesticide effects. In the sections that follow, we elaborate these domains and their linkages, illustrating each with empirical case studies.

2. Pesticide use (Domain 1)

All pesticide-pollinator interactions are causally downstream from pesticide use, a phenomenon governed as much by socioeconomic drivers as by anything belonging to the usual purview of ecotoxicology. The intent of pesticide use is the alleviation of pest pressure. Before a pesticide is available for use, though, it must be discovered and developed by the agrochemical industry, approved by government regulators, and marketed to end users whose information and values influence the final decision of when, where, and how to apply a pesticide. It is critical to recognize that the legitimate need to manage pests underlies the phenomenon of pesticide use, particularly in agriculture and vector control (Oerke and Dehne, 2004; World Health Organization, 2006); accordingly, efforts to protect pollinators from pesticide impacts should reconcile pest control needs with the conservation of pollinators and other non-target organisms, incorporating pollinator conservation into integrated pest management (IPM) frameworks rather than seeing pesticide use per se as an antagonist of conservation (Biddinger and Rajotte, 2015).

2.1. Pest pressure

A pest is "any organism that interferes with the activities or desires of humans" (Norris et al., 2003). Species may acquire pest status by competing with humans for food, transmitting disease, damaging the structural integrity of buildings, undermining natural ecosystems, altering the aesthetics of an environment, or causing direct harm or annoyance to humans. Pest status in a particular environment is a function of three main factors: the density of the pest, the relationship between pest density and damage, and the relationship between pest damage and human values (Stern et al., 1959). Thus, pest status can vary both with changes in the biophysical environment and with changes in economic markets or other systems of human value. For example, the advent of synthetic pesticides in the mid-20th century in the United States made it possible to market unblemished fruits and vegetables. This altered consumer expectations and tightened food quality regulations such that blemished produce became unsalable, with the net effect of further intensifying pesticide use (Pimentel et al., 1993).

While particular species have been eradicated or limited to low densities (Hutchison et al., 2010), total pest losses in agriculture (the beststudied realm of pest management) have remained surprisingly constant since the advent of synthetic pesticides in the mid-20th century (Oerke, 2006). Somewhat more success has been seen in the realm of disease vector management, such as the suppression or eradication of malaria mosquitoes in many regions of the world (Hay et al., 2004). Pest management is a moving target in a changing socio-ecological system: new pest species are introduced, existing pest species evolve resistance, agricultural practices shift, human demand for resources continues to grow, and the climate is changing (USGCRP, 2018). This creates a steady demand for new pest management methods, including novel pesticide chemistries and application technologies.

2.2. Pesticide availability: Development and regulation

The suite of pesticides to which pollinators are potentially exposed varies through time as new products become available and existing products are removed (Atwood and Paisley-Jones, 2017). While the adoption of new pesticides is a responsive process driven by pest pressure dynamics and regulatory changes, the initial discovery and development of new active ingredients is largely prospective, impelled and

constrained by market forces, industry structure, and the technical rigors of the research and development process.

The discovery of new pesticides begins with the chemical synthesis and biological screening of candidate molecules, often aided by computer modeling. On average, 160,000 molecules are synthesized and screened for every one molecule brought to market (Phillips McDougall, 2016). Molecules showing desirable properties in the screening phase may be passed on to the development phase, which requires the larger-scale production and formulation of candidate active ingredients along with an extensive battery of laboratory, semi-field, and field tests evaluating safety and efficacy. For products passing the development phase, test results are compiled into a registration dossier and submitted to regulatory agencies for review, where the product is either granted or denied registration. Only after successful registration can a product finally be commercialized and made available to pesticide users. Based on the most recent estimates, the path from discovery to market for a single active ingredient requires, on average, over 11 years and over U.S. \$286 million, and both these figures have risen steadily from 1995 to 2014 (Phillips McDougall, 2016). Moreover, even after a product has been brought to market, costs can continue to accrue through additional testing stipulated by new regulations or registration review.

Any consideration of the pesticide discovery and development pipeline may also need to acknowledge the recent waves of horizontal and vertical integration between firms in agrochemicals, seeds, biotechnology, and precision farming. These integrations create a global agrochemicals market of which 80% is controlled by four multinational corporations (Phillips McDougall Ltd., 2013). While industry representatives point to a "progressive increase in the number of different chemistries being simultaneously explored as the companies have become larger" (Sparks and Lorsbach, 2017), other investigators observe a "shrinking pipeline" for pesticide discovery and suggest that industry consolidation has reduced the number of active ingredients undergoing research and development by 60% between 2000 and 2012 (Schimmelpfennig et al., 2004; Phillips McDougall Ltd., 2016; Borel, 2017). Increasing concentration and market power can decrease competitive pressure to conduct discovery-oriented research and shunt a greater proportion of research and development toward protecting existing chemical products as they come off patent (Phillips McDougall Ltd., 2013; Clapp, 2017).

The industrial process of pesticide discovery and development is tightly coordinated with government regulation (Fig. 2). Pesticide regulation developed over the course of the twentieth century, initially to set standards for pesticide purity in order to protect applicators from dangerous or ineffective pesticides (e.g., U.S. Insecticide Act of 1910), and later to reduce impacts on human health (e.g., U.S. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) of 1947) and the environment (e.g., U.S. Federal Environmental Pesticide Control Act of 1972) (Fagerstone et al., 1990; Chaffey and Dobozy, 2004; Jas, 2007). The emergence of pesticide regulation has been a global phenomenon, but the scope and focus of regulation varies by country (Pelaez et al., 2013). Beginning in the 1990s there has been increasing harmonization of pesticide regulation between member states of the Organisation for Economic Cooperation and Development (OECD), particularly within economically integrated markets such as among European Union member states (Hussey and Bell, 2004) and North American Free Trade Agreement partners (Chaffey and Dobozy, 2004). Nevertheless, while there exist broad international standards around pesticide regulation through the International Code of Conduct on the Distribution and Use of Pesticides (World Health Organization, 2014), there remains considerable heterogeneity in pesticide regulation, which contributes to different patterns of pesticide use between countries and regions (Schreinemachers and Tipragsa, 2012).

While toxicity to bees has been included in the evaluation of pesticide environmental hazards since the 1970s, there is little evidence that these early evaluations led to significant shifts and restrictions in pesticide use. The first major restriction of pesticide use prompted by concern for pollinator safety occurred in 1999, when France suspended the insecticide fipronil and the neonicotinoid insecticide imidacloprid



* Whether cost-benefit analysis is explicitly incorporated into risk assessment for pollinators varies by country/region.

** Approval may be conditioned on risk-mitigating measures, e.g. restrictions on the environmental conditions under which and/or crops on which the pesticide may be used.

Fig. 2. Generalized schematic of tiered risk assessment for pollinators, with definitions of key terms. Regulatory authorities in Australia, Brazil, Europe, and North America rely on a tiered process for assessing risks to bees from compounds for which exposure is deemed significant (European Food Safety Authority, 2013; US Environmental Protection Agency, 2014; Australian Pesticides and Veterinary Medicines Authority, 2015; *Normative Instruction* 2, 2017). Tier 1 evaluates the potential acute and/or chronic risk to adult/larval bees using standard-ized laboratory studies. If risk estimates exceed regulatory threshold and cannot be mitigated or refined, then higher-tier colony-level studies under confined conditions (e.g., enclosures) may be required at Tier 2. Depending on the need for additional refinement, full-field studies of colonies (Tier 3) may be required. The process is intended to be iterative.

applied as seed treatment to pollinator-attractive sunflower crops (Suryanarayanan and Kleinman, 2014). This was followed by a more extensive European Union-wide moratorium in 2013 on three neonicotinoid insecticides (imidacloprid, clothianidin and thiamethoxam) applied as seed treatments to pollinator-attractive crops (European Commission, 2013); the 2015 withdrawal of registrations of neonicotinoid active ingredients on Tilia shade trees in the state of Oregon (Oregon Department of Agriculture, 2015); and a 2016 policy in the Canadian province of Ontario for restricting the use of neonicotinoid seed treatments (Government of Ontario, 2016). Beginning in 2012, United States Environmental Protection Agency (USEPA), working in collaboration with Health Canada Pest Management Regulatory Agency (PMRA) and the California Department of Pesticide Regulation, developed a conceptual framework for quantifying risks to bees, resulting in the 2014 harmonized Guidance for Assessing the Risk of Pesticides to Bees (US Environmental Protection Agency, 2014). In 2013, USEPA ordered the revision of thousands of pesticide labels to reduce acute exposure of bees to neonicotinoid insecticides at bloom on crops requiring contracted pollination services. Currently, USEPA is employing its new risk assessment process to evaluate four neonicotinoid insecticides as part of the agency's mandated 15-year re-assessment of registered pesticides. In January 2017, USEPA released its Policy to Mitigate the Acute Risk to Bees from Pesticide Products, which affects a broader range of pesticide classes (Fishel et al., 2017), focusing on pesticide use by agricultural applicators when beekeepers are under contract to provide pollination services. The policy also tasks state and tribal lead agencies to develop voluntary Managed Pollinator Protection Plans in order reduce overall pollinator exposure to pesticides. Most recently, the European Union has issued a ban on all outdoor use of neonicotinoid insecticides (The European Commission, 2018a, 2018b, 2018c), citing a European Food Safety Authority report (European Food Safety Authority, 2018) concluding that the compounds pose an unacceptable risk to bees (European Food Safety Authority, 2018).

Finally, the use of pesticides depends not solely on the availability of chemical products but also on the availability and cost-effectiveness of non-chemical alternatives, including cultural (e.g. crop rotation), mechanical (e.g. trapping), biological (e.g. releasing predators/parasitoids), and genetic (e.g. selective breeding, transgenics) techniques. For example, in the management of Hessian fly in wheat, insecticide use has been successfully minimized by the use of resistant cultivars (genetic control) along with cultural and biological control methods (Schmid et al., 2018). Similarly, the management of navel orangeworm in almonds relies principally on the cultural methods of winter sanitation and timing of harvest, with insecticide use as a secondary option that can often be avoided (Almond Board of California, 2011). The relationship between non-chemical alternatives and insecticide use is not always simple, though. The introduction of Bt transgenics (genetic control) in U.S. corn in the 1990s led to a reduction in the mass of insecticides applied (Osteen and Fernandez-Cornejo, 2013; Wechsler and Smith, 2018), but also coincided with an expansion of the total area of corn treated with insecticides via the adoption of neonicotinoid seed treatments (Douglas and Tooker, 2015).

2.3. Information and values

Another approach to understanding current and historic patterns of pesticide use is on the basis of the information and values of pesticide applicators, farmers, land managers, and consumers. Methodologically, this approach involves measuring individual knowledge and values, along with market conditions (e.g., prices, availability), to understand pesticide use outcomes. Some researchers have pointed out that there is frequently a gap between knowledge of environmental problems and the capacity to address them (Blühdorn, 2011; Stoner, 2014; Melathopoulos and Stoner, 2015). One reason for this is that markets for goods with negative externalities, such as pesticides, typically do not value resources comprehensively. Furthermore, pest management practices are continually changing, driven by factors that extend far beyond the decision-making of individual applicators (Friedmann, 1982; Russell, 2004). The complexity of pest management decisions has led some researchers to conclude that complexity itself incentivizes the use of pesticides as a risk mitigation strategy (Castle et al., 2009; Gent et al., 2013). Others have noted that pesticide reduction is most successful when integrated within a broader strategy of regulatory change coupled with the development of effective and reasonably-priced pest control alternatives (Goldberger et al., 2013; Farrar et al., 2016).

A prominent area of research into how knowledge shapes pesticide applicator decision-making centers on the sources of knowledge used by applicators. In the US, the most widely used sources of information on pesticides are crop consultants (Lichtenberg and Zimmerman, 1999; Brodt et al., 2005; Goldberger et al., 2013). Crop consultants are often affiliated with chemical sellers and primarily paid through commission (though there are also independent consultants). In a study of California almond growers, Brodt et al. (2005) found that independent crop consultants communicated more frequently with growers than crop consultants employed by chemical sellers. They also found that growers who use independent crop consultants tend to feel more knowledgeable about integrated pest management (IPM) and report the use of more complex pestmonitoring techniques and control practices than those who use crop consultants employed by chemical sellers. The use of selleraffiliated consultants was also greater among almond growers with smaller orchards, but across all almond growers this particular study did not find that the level of pesticide use differed based on whether the consultant was independent or connected to a seller (Brodt et al., 2005). Nevertheless, increased reliance on industrylinked crop consultants could affect pesticide use decisions in other settings. Public extension services, which are often considered an independent source of information, have experienced a decline in funding over the past several decades (Pardey et al., 2013).

Integrated Pest Management (IPM)-a paradigm that uses knowledge of pest biology and ecology in combination with a diversified suite of pest management methods (including non-chemical methods) to pursue economically viable pest management while minimizing hazard to humans and the environment-has been promoted since the 1970s as a way to reduce pesticide use and associated non-target effects on humans and the environment (Kogan, 1998). Nevertheless, despite considerable investment in establishing decision-making tools and notable examples of success, such as pesticide reduction in cotton production systems in developing countries (Russell, 2004), IPM does not necessarily achieve aggregate reduction in pesticide use (United States General Accounting Office, 2001; Devine and Furlong, 2007; Brewer and Goodell, 2012). This lack of reduction in pesticide use can be attributed to the large amount of uncertainty associated with some pest and disease forecasting models, which encourages prophylactic use of treatments (Epstein and Bassein, 2003), as well as a lack of incentives for researchers to develop better decision-making tools (Hokkanen, 2015). Moreover, since pesticide prices have not risen as sharply as other inputs (e.g., labor), there is an incentive for precautionary pesticide use to avoid other costs (Clark et al., 1998; Mauro and McLachlan, 2008; Castle et al., 2009; Gent et al., 2013). Also, new technologies, particularly incorporation of genes expressing insecticides and herbicide tolerance, as well as seed treatments, emphasize pest or weed prevention and are not clearly compatible with IPM principles (Hokkanen, 2015; Tooker et al., 2017). Finally, there is considerable variation in how IPM adoption and success are defined and measured; some of the lack of success of IPM is likely related to overly broad definitions of IPM (United States General Accounting Office, 2001) or cases in which IPM leads to reductions in particular pesticides of concern (e.g. to human health) without reducing the total quantity of pesticides applied (Epstein and Zhang, 2014).

Consumer concern over pesticide use and pesticide residues in food has resulted in the rapid expansion of the market for organic foods, globally valued at US \$89.7 billion in 2016 (Willer and Lernoud, 2016), as well as the restriction of certain pesticides by some conventional food processors (Epstein and Bassein, 2003). Yet, these concerns notwithstanding, there remains very low tolerance for cosmetic damage to food (Castle et al., 2009), which pesticides help limit. Organic producers are required to avoid the use of synthetic chemicals in crop production and rely instead on biological pest management and nonsynthetic chemicals, such as lime sulfur (Greene et al., 2017). Although natural pesticides are not necessarily safer simply by virtue of being non-synthetic (Magkos et al., 2006), a literature review and metaanalysis by Barański et al. (2014) finds a lower incidence of pesticide residues in organically grown crops.



Fig. 3. Spatiotemporal patterns of pesticide exposure for two hypothetical pollinator species and two hypothetical pesticides. Gridded squares represent pesticide contamination, pollinator activity level, and exposure in a hypothetical landscape at 4 snapshots in time. Exposure at a given time is the product of the overlap of pesticide contamination and pollinator activity. Temporal dynamics (above) are illustrated for a single focal patch (yellow box). Dotted and dash-dotted lines represent the activity level of two hypothetical pollinators, species A and B. Red and blue lines represent contamination levels for two hypothetical pesticides, compounds X and Y. Cumulative exposure is represented conceptually (not quantitatively, since the y-dimensional scaling of activity and contamination is arbitrary) by shaded areas under the contamination curves where they intersect with pollinator activity. A case of simultaneous exposure to compound X is illustrated at time 2 (darker red fill). A case of simultaneous exposure to compound X and Y is illustrated at time 3 (purple fill). In this scheme, cumulative exposure would be the sum of exposure across all spatial units (grid cells) and integrated over all time units.

Case study 1

Responses to new pest pressures in Pennsylvania apple production.

Pennsylvania, USA, has a thriving apple industry with 20,000 acres of apple production raising >100 varieties of apples and generating \$117 million annually in gross revenue (Pennsylvania Pollinator Protection Plan Task Force, 2017; USDA-NASS, 2018). Unlike some crops wholly dependent on managed honey bees for pollination, more than half of Pennsylvania's apple growers, including some large acreage operations, do not rent honey bees but instead rely upon wild bees living in and around the orchards. Recent surveys have demonstrated the commitment of Pennsylvania apple growers to adopting management practices that support wild bee populations and their pollination services (Park et al., 2018).

Motivated to maintain wild bee pollination services, farmers worked with the Pennsylvania State University Fruit Research and Extension Center to design a multi-faceted program that integrates pest management with protection of pollinators–an IPM program in which pollinator conservation is explicit (Biddinger and Rajotte, 2015)–to respond to the region's heavy pest pressure. Pennsylvania apple growers face more than two dozen major insect and mite pests as well as fungal and bacterial pests. The IPM system they designed incorporates biological controls, host plant resistance, pest monitoring and prediction models, as well as highly specific pesticide applications, all with a goal of protecting pollinators and other beneficial arthropods.

This system, however, will need to adapt as regulations change, new pests emerge, and existing pests become resistant to pesticides. When the rosy apple aphid (*Dysaphis plantaginea*), a pest that leads to stunted and deformed fruit, became resistant to the insecticides used for its control, the only commercially viable alternatives were neonicotinoids, a class of insecticides linked with harm to pollinators (Godfray et al., 2015). Penn State researchers developed approaches to manage the aphid while also minimizing risk to bees by using early season application of the least toxic and shortest-lived neonicotinoid on the market (acetamiprid). This approach ensured that the residues of the pesticide would fall below toxic levels by the time the flowers opened, allowing growers to control rosy apple aphid while protecting the wild bees that were pollinating their crops.

The brown marmorated stink bug (BMSB; *Halyomorpha halys*), native to Asia, is a relatively new pest driving management decisions in eastern U.S. apple production. Growers' decisions will be driven at least in part by information provided on effective control, regulation, and the value they place on wild bee pollination services. Regulation plays a role in this decision since the Food Quality Protection Act requires an increased level of protection for childhood exposures to pesticides. That requirement led to restrictions on the use of some broad-spectrum insecticides, thus limiting the pesticide options available to control BMSB in apple production. Remaining options include neonicotinoids and some pyrethroids to which BMSB has not shown resistance. Growers and researchers are designing methods to manage BMSB, including both pesticide recommendations as well as biological controls such as predatory sand wasps (Tribe Bembicini) and parasitic tachinid flies that attack stink bugs.

As apple growers are honing their response to BMSB, they are also preparing for spotted lanternfly (*Lycorma delicatula*), another invasive Asian pest first found in Pennsylvania in 2014. Thus, strategies for pollinator and pest management are constantly evolving. While the emphasis on pollinator conservation in the context of IPM is a promising approach to reconciling pollinator conservation with pest control, it is not a "silver bullet", as evidenced by the vulnerability of even the best-designed IPM programs to novel pest outbreaks. This underscores the opportunity for innovative and responsive collaboration between researchers, extension agents, regulators, industry, and stakeholders to develop and, when necessary, re-establish successful IPM programs.

3. Pesticide exposure (Domain 2)

Spatiotemporal patterns of pesticide use, modified by chemical fate processes, translate into patterns of environmental contamination. These, in turn, can produce spatiotemporal patterns of pesticide exposure via interaction with the life-history traits and activity patterns of pollinators (Simon-Delso et al., 2017) (Fig. 3).

3.1. Pesticide use and environmental fate

Pesticide use as the output of Domain 1 can be understood as an *event* dependent on ecological and societal processes. When pesticide use becomes the input to Domain 2, however, it must be understood as a spatiotemporal *pattern* related to spatiotemporal patterns of organisms and physical processes within agroecological systems.

In agricultural settings, pesticide use varies by crop, resulting in landscape-dependent pesticide use patterns (Yang et al., 2015; Meehan and Gratton, 2016), and corresponding heterogeneity of pollinator exposure (Brittain et al., 2010; Hladik et al., 2016; Tsvetkov et al., 2017). The quality of data documenting agricultural pesticide use patterns varies regionally. The California Pesticide Use Reporting (PUR) program is, to our knowledge, unique in its documentation of per-field pesticide use at an hourly temporal resolution. More commonly, agricultural pesticide use data are available only in spatially and temporally aggregated forms, such as the annual county- and state-level data maintained by the U.S. Geological Survey's Pesticide Synthesis Project. In other cases, data are also aggregated across compounds so that individual active ingredients cannot be traced (European Commission, 2017), and in some regions data may be lacking entirely or not made publicly available. In addition to this variation in precision and availability, pesticide use data vary in the metrics considered, e.g. pesticides sales, amount of land area treated, mass of product applied.

Knowledge of non-agricultural pesticide use (e.g. cosmetic plant protection, vector control, structural pest control) is largely anecdotal, but available evidence suggests that non-agricultural pesticide use is widespread and, when undertaken by non-professionals, frequently in violation of regulation. The United Kingdom's Amenity Pesticide Use survey (Garthwaite et al., 2018) indicates that the use of herbicides in weed control dominates overall non-agricultural pesticide use, but this survey captures only pesticide use by professional applicators. Surveys in California and Minnesota indicate that pesticides-most commonly insecticides-are stored in nearly all residential homes (Adgate et al., 2000; Wilen, 2002; Flint, 2003; Guha et al., 2013), and that while most home pesticide users read labels, the majority do not measure their pesticide applications precisely, and many dispose of unused pesticide improperly (Wilen, 2001, 2002; Flint, 2003). Surface water residue data suggest that the intensity of pesticide use in urban areas may sometimes exceed that of agricultural areas (US Geological Survey, 2007), and for some pesticides, labeled application rate can be much higher for non-agricultural than for agricultural use (Hopwood et al., 2016). Pyrethroid insecticides associated with mosquito abatement were found to be a major contaminant of pollen collected by honey bees in Indiana (Long and Krupke, 2016), and a large bee-kill occurred in South Carolina in 2016 after an aerial application of an organophosphate insecticide was made in response to fears of mosquitoborne Zika virus (Guarino, 2016). A comparison of bumble bee pesticide exposure in urban and agricultural landscapes in the U.K. found that, while overall pesticide exposure was higher in agricultural landscapes, bumble bees in urban landscapes exhibited high levels of certain pesticides, particularly neonicotinoid insecticides (Botías

et al., 2017). Cosmetic use of neonicotinoids on *Tilia* trees has led to documented bumble bee kills, including one incident in Oregon in 2013 when the use of dinotefuran on flowering *Tilia* trees killed an estimated 50,000 bumble bees (Xerces Society, 2013). Thus, while patterns linking landscape composition to non-agricultural pesticide use may be difficult to ascertain, available evidence suggests that pollinators may be impacted by such use, and systematic study of non-agricultural pesticide use is lacking.

Patterns of pesticide use, however, provide only a snapshot of pesticides in the environment. Once applied, a pesticide is subject to environmental fate processes that determine its movement and persistence in the environment. Thus, the patterns of environmental contamination with which pollinators potentially intersect are both spatially and temporally dynamic, determined by interactions between pesticide use patterns, environmental conditions (e.g. temperature, moisture, microbial activity, soil composition), and the physicochemical properties (e.g. hydrophilicity, volatility, reactivity) of the pesticides applied (Flury, 1996; Arias-Estévez et al., 2008; Bonmatin et al., 2015).

3.2. Pollinator behavior and life history

Pesticide use, fate dynamics, and environmental conditions determine the spatiotemporal patterns of pesticide contamination in the environment. Connecting patterns of contamination to patterns of pollinator exposure, however, requires an understanding of the behavioral and life history traits that govern the interactions between pollinators and their environment, and hence the spatiotemporal intersection between pollinators and environmental contaminants (Sponsler and Johnson, 2017; Kopit and Pitts-Singer, 2018).

3.2.1. General behavioral and life history traits

Pollinator behavioral traits can be parsed in many ways, but we highlight four trait classes that are especially relevant to pesticide exposure: foraging behavior, nesting behavior, phenology, and sociality.

Foraging behavior in pollinators varies in terms of localization (central-place vs. non-central-place), range (<100 m to >10 km), and diet breadth (ranging from highly specialized to highly generalized). An important corollary of non-central-place foraging is that juveniles, lacking a nest, are free-foraging rather than provisioned by adults, multiplying potential routes of juvenile pesticide exposure. Foraging range, strongly correlated with body size in bees (Greenleaf et al., 2007), influences how much of the environment a pollinator interacts with and, therefore, its extent of intersection with environmental contaminants. Diet breadth similarly constrains environmental interactions. It is likely that long foraging range and broad diet breadth, as exemplified by honey bees, contribute to simultaneous exposure to multiple pesticides (Mullin et al., 2010), but these traits may also have the effect of diluting dietary pesticide exposure by the combination of contaminated and uncontaminated sources (Baveco et al., 2016). Conversely, shorter foraging range and narrower diet breadth make pesticide exposure dependent, for better or worse, on a smaller subset of the environment. It must be noted, though, that both foraging range (Couvillon et al., 2014) and diet breadth (Fontaine et al., 2008) can vary facultatively based on resource availability.

In pollinators that form nests, nesting behavior includes wax comb construction (honey bees, bumble bees (*Bombus spp*), stingless bees), subterranean burrows (non-*Apis* bees and wasps), above-ground cavities (non-*Apis* bees and wasps), and various uses of leaves and flowers (e.g. nest cell lining in Megachilid leafcutter bees), wood pulp (e.g. carton nest construction by social wasps), and plant resins (e.g. nest sealing honey bees and resin bees). Each of these nesting substrates presents a potential source of pesticide exposure (Kopit and Pitts-Singer, 2018).

In terms of phenology, the majority of pollinators have discrete seasonal activity periods, but some remain active throughout the

Table 1

Summary of behavioral and life history traits of selected insect pollinators.

	Foraging							Nesting		Phenology		Sociality			
Guild	Localization		Range (m)			Diet breadth									
	CP†	non-CP	<500	500-3000	>3000	specialist	generalist	wax	soil	plant	seasonal	continuous‡	nonsocial	weakly social	highly social
honey bees															
stingless bees															
bumble bees															
other bees															
social wasps															
solitary wasps															
other insect pollinators*			NA	NA	NA			NA	NA	NA					
*principally flies, butterflies and beetles: taxa distinguished by non-central-place foraging behavior and free-foraging larvae															

†central-place

‡may refer either to perennial colonies (e.g. honey bees) or annual colonies that are active throughout all or most of the growing season (e.g. bumble bees)

*Principally flies, butterflies and beetles: taxa distinguished by non-central-place foraging behavior and free-foraging larvae. †Central-place.

#May refer either to perennial colonies (e.g. honey bees) or annual colonies that are active throughout all or most of the growing season (e.g. bumble bees).

1020

growing season (bumble bees and certain wasps, flies, and butterflies) or even perennially active (honey bees, stingless bees, and certain wasps). Analogous to the relationship between foraging range, diet breadth, and spatial interaction with the environment, a pollinator's phenology determines the temporal interval of the environment with which it interacts, and where this interval falls with respect to the timing of pesticide application is critical for determining exposure.

Finally, while most pollinators are solitary, some species live in social groups. Social behavior has been characterized extensively in bees (Michener, 1969) and wasps (Ross and Matthews, 1991), but for the purposes of the present discussion pollinators can be coarsely classified as nonsocial (either strictly solitary or weakly associated), weakly social (e.g bumble bees), or highly social (e.g. honey bees). In nonsocial pollinators, pesticide exposure depends only on the behavior of the individual. In social species, nestmates share common food stores, meaning that dietary pesticide exposure is potentially both propagated and diluted. In most advanced social species, like honey bees, the extent of food sharing is such that the colony can be described as sharing a "common stomach" (Schmickl and Karsai, 2017), which may buffer individuals against high pesticide exposure while ensuring that virtually no colony members escape exposure entirely (Sponsler and Johnson, 2017).

Given the estimated 347,000 insect pollinator species (Ollerton, 2017), a general inquiry into the link between pollinator behavior and pesticide exposure benefits from the aggregation of major pollinator species into trait-based guilds. An example of this approach is shown in Table 1, where major insect pollinator groups are grouped into seven categories. This classification, while intended as a preliminary illustration of concept, immediately suggests some practical generalizations. For example, highly social honey bees and stingless bees differ from their less social pollinators not only in sociality but also in nesting substrate, with implications for potential exposure routes (Kopit and Pitts-Singer, 2018). For the minority of pollinators with continuous activity, studying exposure with respect to temporally aggregated pesticide use may be warranted, but for the majority of species, specifying the temporal intersection between pollinator activity and pesticide use is indispensable. Non-central place pollinators present qualitatively different challenges in studying pesticide exposure, since they are not tied to any particular landscape, their larvae are free-foraging, and they are phylogenetically diverse and far removed from their Hymenopteran counterparts.

3.3. Patterns of exposure

Thus far, our discussion of exposure has emphasized the practical need for generalization, both of pesticide use patterns as a function of landscape (3.1) and of pollinator behavior and a life history (3.2). Such generalizations are helpful and necessary for broad heuristics and for the design of multi-species risk assessment schemes (European Food Safety Authority, 2013). In any particular exposure scenario, however, it is the specifics of pesticide use and pollinator behavior that determine exposure. Fine-scale questions must be answered: which pollinator taxa are conservation priorities, where is the intersection between pesticide application and pollinator-attractive flora, how does the timing of pesticide application relate to the seasonal and daily activity of pollinators (Fig. 3)? The specific patterns of exposure-timing, duration, combinations of compounds-that arise from these fine-scale interactions are instrumental in determining pesticide effects, and their study is one of the most challenging frontiers of pesticidepollinator science.

Case study 2

Pollinator exposure to seed treatment neonicotinoids.

In 2008, a nascent invasion of the western corn rootworm (Diabrotica virgifera virgifera, LeConte) in Germany (Hummel et al., 2005) prompted an emergency authorization of the neonicotinoid insecticide clothianidin to be applied at a high rate (125 g/ha) as a seed treatment in corn (Forster, 2009). During the planting of clothianidin-treated corn, honey bee (Apis mellifera) poisoning incidents were reported, affecting over 11,000 colonies, and clothianidin was soon confirmed to be the causal agent (Forster, 2009; Pistorius et al., 2009). This prompted an investigation into the question of how bees could be exposed to a seed treatment insecticide during the planting process, and the results of that investigation illustrate the importance of understanding the spatiotemporal patterns of pesticide use, environmental fate, and pollinator activity. The spring of 2008 exhibited a climatic anomaly that caused oilseed rape and other bee-attractive crops, frequently located adjacent to corn fields, to bloom simultaneously with corn planting (Forster, 2009; Nikolakis et al., 2009). Thus, the spatiotemporal distribution of foraging bees was brought into alignment with the spatiotemporal distribution of clothianidin use. But even so, how is it that foraging bees could be exposed to a pesticide adhered to seeds? This is a question of environmental fate. During the planting process, the seed treatment material sloughed off the seed surface and became mobilized as small, airborne particles (Pistorius et al., 2008), a phenomenon first documented by Greatti et al. (2003). In the German incident, the dispersal of these particles was aided by unusually dry and windy conditions (Forster, 2009; Nikolakis et al., 2009) and further exacerbated by quality control shortcomings during the initial application of the seed treatments (Nikolakis et al., 2009). Subsequent research would show that these particles both drift onto neighboring vegetation and form plumes of toxic dust in the immediate vicinity of running planters (Krupke et al., 2012; Girolami et al., 2012), generating both floral contamination and aerial contact routes of exposure for foraging bees. While an incident of comparable magnitude to the German bee kill of 2008 has not been documented since, incidents of honey bee mortality during the planting of neonicotinoid-treated corn seed have been reported in France (Alix et al., 2009), Slovenia (Alix et al., 2009; van der Geest, 2012), Italy (Bortolotti et al., 2009), the U.S. (Krupke et al., 2012), and Canada (Health Canada, 2013). Moreover, several additional routes of exposure have been identified, including the movement of seed-applied neonicotinoids into the surrounding soil and nearby growing flowering weeds (Krupke and Long, 2015).

4. Pesticide effects (Domain 3)

Having explored the more obscure domains of pesticide use and exposure, we come now to pesticide effects, the domain of pesticide-pollinator science that enjoys by far the richest empirical support. Even here, though, our knowledge is incomplete, particularly with respect to linking organismal effects to higher-order effects on colonies, populations, and ecosystems, and understanding whether and how these effects feedback, by accident or design, upon the pesticide use drivers of Domain 1.

4.1. Toxicity and effects on individual pollinators

Pesticides can exert sublethal and lethal effects on individual pollinators, and the type and extent of these effects vary with exposure level, duration, and route (ingestion, contact, inhalation) (see Domain 2); the mode of action of the pesticide; interactions between pesticides; the developmental and physiological state of the pollinator; and the species of pollinator. Moreover, these effects are not caused only by insecticides specifically designed for insect toxicity; other pesticides, such as fungicides and herbicides, can also be toxicologically relevant to pollinators. Furthermore, many adjuvants included in pesticide formulations can synergize active ingredients or even possess intrinsic toxicity (Mullin, 2015), with documented effects including impaired learning and memory (Ciarlo et al., 2012) and increased viral titers (Fine et al., 2017). Published studies of the "inert" ingredients in formulations are quite limited, though, so we will focus our review on active ingredients.

The most commonly used insecticides are neurotoxic compounds, such as organophosphates, carbamates, pyrethroids, phenylpyrazoles, and neonicotinoids. Organophosphates and carbamates are potent inhibitors of the enzyme responsible for deactivating acetylcholine (acetylcholinesterase, AChE); pyrethroids destabilize the voltage-gated sodium channels within neurons; fipronil blocks the γ -aminobutyric acid (GABA) and glutamate gated chlorine channels; and neonicotinoids bind to the postsynaptic nicotinic acetylcholine receptors (nAChRs). In every case, there is over-stimulation of the nervous system leading to loss of coordination, paralysis, and death. Certain fungicides can also be harmful to pollinator health, although the exact mechanism of action is unknown. For example, the fungicide captan, which inhibits cell division in a broad spectrum of fungi, can be acutely toxic to Osmia lignaria at field relevant concentrations (Ladurner et al., 2005) and can induce larval mortality and developmental malformations in honey bees (Atkins and Kellum, 1986; Mussen et al., 2004), while the fungicide boscalid can lead to chronic and cumulative toxicity in adult honey bees (Simon-Delso et al., 2018). Indirect effects of fungicides on pollinators include alteration of patch-level floral displays in some plant species due to impacts on mycorrhizae, which can in turn alter pollinator visitation (Cahill Jr et al., 2008). As for herbicides, although they target physiological pathways specific to plants, they have the potential to interfere with metabolic and reproductive processes in pollinators as well. For instance, paraguat is highly toxic to honey bees when applied topically (Moffett et al., 1972) and 2,4-D and 2,4-trichlorophenoxyacetic acid can negatively influence brood development (Morton and Moffett, 1972). The herbicide glyphosate targets a pathway (5enolpyruvylshikimate-3-phosphate synthase) found not only in plants but in certain bacteria of the gut microbiome of honey bees, and exposure to glyphosate under laboratory conditions can perturb honey bee gut microbiota (Motta et al., 2018), impair honey bee larval development (Dai et al., 2018; Vázquez et al., 2018), and alter various aspects of behavior and physiology (Herbert et al., 2014; Helmer et al., 2015). The primary impact of herbicides on pollinators, however, is their negative effect on the availability of flowering plants, reducing pollinators' nutritional resources and potentially exacerbating the impacts of other stressors (Freemark and Boutin, 1995; Bohnenblust et al., 2016).

As there are a broad range of pesticides in use, pollinators are often not exposed to a single pesticide alone but receive multiple exposures, both simultaneously and in sequence, to a cocktail of chemicals arising from both agricultural and non-agricultural use (Mullin et al., 2010; Berenbaum, 2016; Long and Krupke, 2016) with some combinations producing greater than additive effects. For example, the toxicity of certain insecticides (e.g. neonicotinoids and pyrethroids) can be enhanced in the presence of demethylation-inhibiting (DMI) fungicides (e.g. epoxiconazole, tebuconazole, prochloraz) (Pilling et al., 1995; Iwasa et al., 2004; Sgolastra et al., 2017) because the fungicide inhibits the P450 enzymatic detoxification mechanism such that the insecticide residues are metabolised more slowly. This effect is dose dependent, however, and the magnitude of synergism in field exposure scenarios is uncertain (Thompson et al., 2014). Likewise, some acaricides routinely used to control Varroa mites in honey bee hives, which are detoxified by P450s (e.g. tau-fluvalinate, coumaphos, and fenpyroximate), may interact with P450-inhibiting DMI-fungicides, potentially increasing toxicity due to additive or synergistic effects (Johnson et al., 2013). Therefore, the real toxic challenge encountered by pollinators in the field may be hard to predict from single-compound laboratory studies.

4.2. Propagating effects to colonies, populations, and systems

Effects on individual pollinators can result in higher-order effects on colonies (in the case of social species) and populations of both social and solitary species, potentially leading to ecosystem-scale effects on pollination services, pollinator biodiversity, and apicultural productivity. The propagation of effects through these levels of organization is arguably the most difficult aspect of pesticide-pollinator science, or indeed of toxicology at large, but also one of the most important, for these higher orders of effect are where human interest is most vested, where ecological function is most at stake, and where regulatory criteria are defined.

Ankley et al. (2010) formalized an "adverse outcome pathway" for ecological risk assessment that involves identifying an impact at a lower level of organization (such as a change in activity of biosynthetic enzymes, neurons, or key signaling pathways) that can predict outcomes at a higher level of organization. Quantitatively linking changes at one level of organization (e.g., changes in enzymatic activity) to another (e.g., crop pollination) is, however, extremely challenging (Rohr et al., 2016). First, even the impact of a pesticide with a well-defined molecular target in an individual organism can have unexpected impacts: for example, neonicotinoids primarily interfere with neuronal



Fig. 4. Priorities for pesticide-pollinator scholarship. Priorities 1–3 pertain to their respective domains, while priority 4 integrates across domains and transcends the boundaries of the system.

activity, but sublethal exposure to neonicotinoids can impair immune responses and lead to increased viral titers in honey bees (Di Prisco et al., 2013). Second, it is difficult to predict the type and magnitude of change that needs to occur at one level of organization (e.g., molecular) to impact consistently a higher level of organization (e.g., population). Third, there are many factors that can modulate the likelihood and magnitude of an adverse effect that exposure to a pesticide may have on an individual or social group, such as how hard an organism has to work for its food (Mommaerts et al., 2010) or the type of landscape it inhabits (Park et al., 2015), and it is challenging to quantify accurately all these factors in the environment and integrate them into a predictive model.

To illustrate the importance and difficulty of translating pesticide effects across different levels of biological organization, one can consider the well-studied phenomenon of pesticide effects on the foraging behavior of bees and how these effects may lead to cascading effects at other levels of biological organization, including impacting ecological outcomes that are relevant to stakeholders, regulators, and the public. High exposures to pesticides can cause acute mortality of foraging bees, while lower levels of exposure can impair foraging bees' ability to locate nectar and pollen resources and return them to the nest (Gill et al., 2012; Feltham et al., 2014; Balbuena et al., 2015). Moreover, exposure of developing brood to pesticides can reduce foraging ability and lifespan of adult bees (Tsvetkov et al., 2017). This can reduce the reproductive output of solitary bees, as the offspring are entirely dependent on the foraging activities of their mother (Zurbuchen et al., 2010), as well as in social bees with smaller colonies such as bumble bees (Rundlöf et al., 2015). For social bees, the colony can, to some extent, compensate for a loss of foragers or reduced intake of food by recruiting additional bees to the foraging force (Barron, 2015) or reinvesting reproductive output in new workers (Henry et al., 2015). However, as has been demonstrated for honey bees, these newly recruited bees are not as efficient as experienced foragers and may be more subject to predation, necessitating the recruitment of even more new foragers (Perry et al., 2015). Thus, if a colony is exposed to pesticides over a long period of time, these processes can lead to small colonies that do not reach a sufficient size to produce reproductives or survive harsh conditions (such as winter). A severe imbalance of colony demographics may even result in collapse of the colony (Barron, 2015).

Tracing these effects to the levels of population or ecosystem, however, is more challenging. In this regard, the best-studied scenario is bee exposure to neonicotinoid insecticides, though it must be acknowledged at the outset of this discussion that the effects of neonicotinoid exposure above the level of the individual-and the ability to measure these effectsare contingent on multiple and interacting drivers, and many field-scale studies have found no detectable effects (Godfray et al., 2014, 2015). We focus on studies where effects were detected so as to demonstrate the potential for effects propagation while acknowledging that none of these studies establishes a universal cause-and-effect relationship. Experimental studies using field-based exposure have found a significant reduction in reproductive output in solitary bees and colony size and reproductive output in bumble bees (Rundlöf et al., 2015; Woodcock et al., 2017). Whether these produce true population responses is not certain, but such measures of demographic parameters are, in most cases, the closest proxy available for measures of population response. Effects on honey bee colonies are more variable, and likely dependent on other drivers of colony health (Rundlöf et al., 2015; Woodcock et al., 2017), although a long-term study of trends in the U.K. found a correlation between honey bee colony losses and imidacloprid seed treatments of oilseed rape (Budge et al., 2015). Similarly, long-term population declines have been observed in wild bee species preferentially feeding on crops that use neonicotinoid seed treatments, relative to other bee species (Woodcock et al., 2016). In terms of ecosystem services, bumble bee colonies exposed to sublethal field-relevant concentrations of neonicotinoids provided lower pollination services to apple, likely a result of an overall reduction in foraging force (Stanley et al., 2015). In some cases, however, insecticide use is associated with declines in pollinator abundance while at the same time pollination services to focal crops are increased (Brittain et al., 2010). Thus, the impact on crop yield is an interaction between pollinators and pest control (Lundin et al., 2013; Melathopoulos et al., 2014). Moreover, the economic consequences even of severe pollinator losses may be difficult to predict, as evidenced by the apparent robustness of most pollinator-dependent crop markets in the U.S. to high annual loss rates in managed honey bees (Ferrier et al., 2018). Such complex articulation of ecological with economic drivers underscores the necessity of transdisciplinary science and responsive dialogue between scientists, policymakers, agricultural practitioners, and the public.

Case study 3

Voluntary adoption of pollinator best management practices by California almond growers.

Can an understanding of pollinators' value to crop production and the risks of pesticide exposure to pollinator health (Domain 3) induce changes in pesticide use practices (Domain 1)? California almond is the largest pollinator-dependent crop in North America, relying on over 2 million managed honey bee colonies annually to pollinate over 1,000,000 acres of bearing orchards. As in the case of Pennsylvania apples, growers are keenly aware of the dependence of yield on pollination services provided by bees. The Almond Board of California-in collaboration with beekeepers, regulators, registrants, the non-profit organization Project Apis m., and University of California Cooperative Extension-developed self-regulated best management practices (BMPs) that lay out practical steps almond growers can take together with beekeepers to promote bee health on their orchards and in the surrounding landscapes (Almond Board of California, 2014). Although these BMPs include a range of elements, a major focus is the reduction of pesticide exposure of bees in orchards. In addition to basic steps like avoiding prophylactic pesticide use and minimizing direct spraying of bees while on the crop, the BMPs exemplify consideration of bee behavior (Domain 2) by stipulating that clean water sources (used by honey bees to thermoregulate their colonies) be provided in orchards while honey bee colonies are present. The BMPs also account for the importance of information and values in driving human decision-making (Domain 1) by using multi-tiered implementation and information transfer to reach as broad an audience as possible and encourage widespread adoption. BMPs are presented over multiple years at annual industry conferences, guidelines are provided in condensed form for in-field reference, and specific applicator sheets are provided in streamlined form in multiple languages. Throughout, a central emphasis is the importance of communication between beekeepers and growers in the design and implementation of pest management plans.

The development of these BMPs has improved both communication between stakeholders and in-orchard conditions for managed honey bees, with grower sustainability surveys showing that 94% of growers coordinate pest control with their beekeepers and 93% of growers provide clean water for bees while they are present in the orchard (Almond Board of California, 2017). Several factors favored the development and successful adoption of BMPs within the almond context: (1) growers and beekeepers most often have contractual agreements under which hives are rented for pollination, encouraging mutual accountability; (2) the State maintains mandatory reporting records of pesticide (including insecticide, fungicide, herbicide) application by commercial farms from the smallest community-supported agriculture operations to the largest corporations, thus there is accountability and traceability related to potential exposure; (3) bees are in high demand so poor compliance (exposure of bees) by growers might jeopardize future pollination services; (4) beekeeper livelihood strongly depends on the almond pollination event so beekeepers are highly motivated to work with the growers and BMPs provided.

5. Application and conclusion

The science of pesticides and pollinators suffers from vast gaps, not just in data but in theory, communication, and practice. A new generation of pesticide-pollinator scholarship could provide both a synthesis and set of applications, informed by the structured relationships depicted in our framework. Specifically, we highlight four possible priorities (Fig. 4). Following Stember's (Stember, 1991) typology, priorities 1–3 are domain-specific and can be undertaken with approaches ranging from intradisciplinary to interdisciplinary, while priority 4 transcends not only our domain boundaries, but even the boundaries of our overall framework, requiring fully transdisciplinary scholarship.

5.1. Priority 1: Stakeholder engagement

Calls for action regarding pesticides and pollinators tend to emphasize the need for research and regulation. As our framework makes clear, though, pesticide effects on pollinators lie downstream from the legitimate need of stakeholders to manage pests, the management options available to them, and the factors influencing their decisions. The framework highlights the importance of developing diverse and effective pest management techniques that meet stakeholder needs while minimizing risk to pollinators and other non-target organisms (Biddinger and Rajotte, 2015). Such efforts to balance multiple objectives could benefit from engaging stakeholders in ways that are more inclusive of their expertise and attentive to historically shaped dynamics of power, conflict and cooperation between university scientists, beekeepers, farmers, and chemical industry representatives (Suryanarayanan, 2015). In the U.S., stakeholder engagement often occurs through public extension services, which have experienced declines in funding and to a lesser extent in personnel over the past several decades (Pardey et al., 2013). Comprehensively addressing the pesticide-pollinator relationships illustrated in this paper may broaden the focus of pollinator extension services to include pollinator health in addition to issues related to apiculture and crop pollination, as was the case in Oregon in 2016 with the creation of a pollinator health extension position at Oregon State University. Interinstitutional bodies that span the diverse domains needed to address pollinator health may help further facilitate an exchange of information and expertise at national or regional levels. In all these cases, however, the ability of these extension efforts to document a reduction of pollinator exposure to pesticides while achieving effective pest management will be critical for informing policy-makers looking to address existing conflicts around pollinators (Melathopoulos and Sagili, 2016).

Amid the decline of public extension services and the concomitant rise of industry-linked private consulting, there has also been an increasing role of non-governmental organizations (NGOs) that advise land managers around pollinator health. The growth and influence of these initiatives over the past decade signal the importance of these actors in helping land managers to reduce non-target pesticide exposure. More work needs to be done to understand how NGOs and more traditional extension services might work together to provide land managers with financially disinterested consultation while providing appropriate forms of accountability to industry-linked private consultants. Given appropriate accountability measures, there may also be a legitimate role of industry-linked consultants in guiding the safe and effective use of their products and encouraging ecological stewardship more broadly.

5.2. Priority 2: Mechanistic exposure modeling and descriptive natural history

At present, pesticide use (Domain 1) and pesticide effects (Domain 3) are held together tenuously by the complex and relatively obscure phenomenon of pesticide exposure (Domain 2). The science of exposure is still crude for honey bees (Sponsler and Johnson, 2017), nascent at best for wild bees (Kopit and Pitts-Singer, 2018), and practically non-existent for non-bee pollinators. The key to elucidating the mechanisms of

pollinator pesticide exposure is understanding it not as a simple event but as a complex intersection of spatiotemporal patterns. One promising way forward is the development of mechanistic simulation models to formalize the heuristics of exposure and enable in silico prediction and experimentation at scales infeasible for field studies. Some early progress has been made in this effort (Baveco et al., 2016), and ongoing efforts are underway (Rortais et al., 2017). Much can be learned by looking outside the field of pollinator ecotoxicology to find examples of mechanistic exposure models in other organisms, including both wildlife (Pastorok et al., 1996) and humans (Loos et al., 2010). Perhaps less obvious, but no less important, is the need for renewed emphasis on descriptive natural history (Tewksbury et al., 2014), particularly of pollinator species representative of functional guilds (Table 1). Computational modeling is built on the foundation of descriptive natural history, and a deficit of the latter with respect to the majority of pollinator species and plant-pollinator relationships leaves modelers with the difficult task of simulating behavior that has yet to be described.

5.3. Priority 3: Mechanistic effects modeling and longitudinal monitoring

The most salient challenge of Domain 3 is understanding the propagation of effects across levels of organization, from the molecular level at which pesticides exert their direct effect to the ecosystem level at which protection goals are defined. This can be understood as an extension of the adverse outcome pathway framework (Ankley et al., 2010) to system-level outcomes beyond the levels of organism and population. In regulatory language, this is the challenge of linking measurement endpoints to assessment endpoints to protection goals (Fig. 2). Effects propagation is a challenging topic to study empirically, though there are notable examples of studies that have successfully linked effects across levels of organization (Rundlöf et al., 2015; Tsvetkov et al., 2017; Overmyer et al., 2018). A promising complement to empirical effects propagation studies is in silico mechanistic effects modeling (Becher et al., 2013; Henry et al., 2017). There is a relatively long tradition of honey bee colony modeling (Becher et al., 2013), culminating recently in the versatile BEEHAVE model, which can incorporate pesticide exposure alongside a broad suite of other stressors to influence colony demographics, productivity, and survival (Becher et al., 2014; Rumkee et al., 2015; Thorbek et al., 2017). Colony- and population-level bumble bee modeling has also undergone a recent renaissance (Bryden et al., 2013; Crone and Williams, 2016; Cresswell, 2017; Banks et al., 2017; Becher et al., 2018). Mechanistic effects models for other insect pollinators, though, have lagged behind. Particularly useful could be models focusing on colony-level effects in stingless bees, which provide valuable pollination services in many tropical systems (Meléndez Ramírez et al., 2018), and population-level effects in solitary bees, which comprise the vast bulk of global bee biodiversity (Michener, 2000) and may be likely more vulnerable to pesticide-driven decline than their social counterparts (Rundlöf et al., 2015). An even greater challenge will be extending these modeling efforts from colonies and populations to the ecosystemlevel outcomes of biodiversity, pollination services, and apicultural productivity. Due to its trans-domain scope, we will return to this challenge in the context of Priority 4.

Analogous to the relationship between exposure modeling and descriptive natural history, population-level modeling relies on longterm monitoring data of pollinator populations (Lebuhn et al., 2013; Goulson et al., 2015). While the costs of long-term monitoring programs are not trivial, they may be justified by the economic and ecological importance of pollinators (Lebuhn et al., 2013) and by the high demand for monitoring data from both research and regulatory communities (Lindenmayer and Likens, 2010).

5.4. Priority 4: Full-cost accounting

Full-cost accounting is an approach that aims to make explicit (though not necessarily to monetize) the total effect of a phenomenon on the network of values in which it participates. For example, a grower's decision to apply pesticides typically balances the benefits provided to the grower against the costs they incur, i.e. a private decision based only on costs and benefits to the grower. These decisions, however, may not account for the full suite of goods and services that are influenced by the use of pesticides, i.e. the externalities, and it is these externalities that full-cost accounting aims to elucidate. With IPM approaches (Case studies 1 and 3), farmers may generate positive externalities (e.g. regional pollinator biodiversity, pollination service availability, apicultural production) while incurring all costs themselves. In contrast, conventional pesticide use may achieve favorable outcomes for individual farmers while failing to account for negative external impacts on regional pollinator diversity, pollination services, and apiculture. This ecological and economic interdependence among farmers, beekeepers, and wild pollinators complicates farmer incentives to adopt IPM practices, but also generates opportunities for cooperative action among stakeholders, potentially catalyzed by government regulation and/or incentivization, to increase net social benefits relative to management based on private returns alone (Grogan and Goodhue, 2012). Moreover, full-cost accounting is useful not only to pesticide users but also pesticide regulators, for the restriction of pesticide use also carries externalities. For example, some have pointed out that the simple banning of neonicotinoids might, in some systems, have the unintended consequence of increasing pest pressure and encouraging the use of older pesticide chemistries and application techniques that may pose a higher risk to pollinators and other non-target organisms (Biddinger and Rajotte, 2015).

5.5. Pollinators and pesticides in context

We acknowledge that the focus of our discussion on the relationship between pesticides and insect pollinators may seem arbitrarily narrow, given that pollinator declines (Ollerton, 2017) may be nested not only within larger patterns of insect decline (Hallmann et al., 2017) but within a global biodiversity crisis that has been characterized as the "sixth mass extinction event" in Earth's geological history (Ceballos and Ehrlich, 2018). Indeed, the scope of potential effects of pesticides on biodiversity and ecosystem function extends far beyond insect pollinators, and we encourage work throughout the whole of this scope. Nevertheless, insect pollinators are an ideal suite of conservation focal species, simultaneously filling the roles of flagship species (evoking public support), umbrella species (having conservation needs that incidentally protect other species), indicator species (sensitive to change/degradation), and keystone species (having ecological impact disproportionate to their abundance) (Caro and O'Doherty, 1999). While pollinator "tunnel vision" must certainly be avoided, a strategic focus on pollinators and their relationship to pesticides appears to be justified.

Finally, we acknowledge the importance of considering pollinator health outcomes in combination with other objectives of environmental health and human wellbeing, among which disease control, food security, and worker safety are preeminent. In the case of pollinator conservation vis-a-vis pesticide use, the applicability of fullcost accounting cuts both ways, meaning that comprehensive analyses must consider not only the effects of pesticides on pollinators, but also the trade-offs between pollinator conservation and other reasonable objectives (Samnegård et al., 2018). The IPM paradigm provides a valuable framework in which to balance the needs of pollinators and people. While science can elucidate the nature of the trade-offs, how to balance pollinator conservation with other objectives (and how to pay for it) is ultimately a decision that must be made adaptively within an extended peer community (Funtowicz and Ravetz, 1993) that includes all relevant stakeholders and decision makers.

Acknowledgments

This work was supported by the National Socio-Environmental Synthesis Center (SESYNC) under funding received from the National Science Foundation DBI-1639145 and by the intramural research program of the U.S. Department of Agriculture, Economic Research Service. Any use of trade, product, or firm names are for descriptive purposes only and do not imply endorsement by the U.S. Government. The findings and conclusions in this preliminary publication have not been formally disseminated by the U. S. Department of Agriculture and should not be construed to represent any agency determination or policy. We thank R. A. Erickson and four anonymous reviewers for helpful critique of our manuscript.

References

- Adgate, J.L., Kukowski, A., Stroebel, C., et al., 2000. Pesticide storage and use patterns in Minnesota households with children. J. Expo. Anal. Environ. Epidemiol. 10, 159–167.
- Alix, A., Vergnet, C., Mercier, T., Others, 2009. Risks to bees from dusts emitted at sowing of coated seeds: concerns, risk assessment and risk management. Julius-Kühn-Archiv 131–132.
- Almond Board of California, 2011. California Almond Sustainability Program: Pest Management.
- Almond Board of California, 2014. Honey Bee Best Management Practices for California Almonds.
- Almond Board of California, 2017. Almond Almanac. p. 2017.
- Ankley, G.T., Bennett, R.S., Erickson, R.J., et al., 2010. Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment. Environ. Toxicol. Chem. 29, 730–741.
- Arena, M., Sgolastra, F., 2014. A meta-analysis comparing the sensitivity of bees to pesticides. Ecotoxicology 23, 324–334.
- Arias-Estévez, M., López-Periago, E., Martínez-Carballo, E., et al., 2008. The mobility and degradation of pesticides in soils and the pollution of groundwater resources. Agric. Ecosyst. Environ. 123, 247–260.
- Atkins, E.L., Kellum, D., 1986. Comparative morphogenic and toxicity studies on the effect of pesticides on honeybee brood. J. Apic. Res. 25, 242–255.
- Atwood, D., Paisley-Jones, C., 2017. US EPA Pesticides Industry Sales and Usage 2008–2012. US Environmental Protection Agency.
- Australian Pesticides and Veterinary Medicines Authority, 2015. Roadmap for Insect Pollinator Risk Assessment in Australia.
- Balbuena, M.S., Tison, L., Hahn, M.-L, et al., 2015. Effects of sublethal doses of glyphosate on honeybee navigation. J. Exp. Biol. 218, 2799–2805.
- Banks, H.T., Banks, J.E., Bommarco, R., et al., 2017. Modeling bumble bee population dynamics with delay differential equations. Ecol. Model. 351, 14–23.
- Barański, M., Średnicka-Tober, D., Volakakis, N., Seal, C., Sanderson, R., Stewart, G.B., Benbrook, C., Biavati, B., Markellou, E., Giotis, C., Gromadzka-Ostrowska, J., 2014. Higher antioxidant and lower cadmium concentrations and lower incidence of pesticide residues in organically grown crops: a systematic literature review and metaanalyses. Br. J. Nutr. 112 (5), 794–811.
- Barron, A.B., 2015. Death of the bee hive: understanding the failure of an insect society. Curr. Opin. Insect Sci. 10, 45–50.
- Baveco, J.M., Focks, A., Belgers, D., et al., 2016. An energetics-based honeybee nectarforaging model used to assess the potential for landscape-level pesticide exposure dilution. PeerJ 4, e2293.
- Becher, M.A., Osborne, J.L., Thorbek, P., Kennedy, P.J., Grimm, V., 2013. REVIEW: towards a systems approach for understanding honeybee decline: a stocktaking and synthesis of existing models. J. Appl. Ecol. 50, 868–880.
- Becher, M.A., Grimm, V., Thorbek, P., et al., 2014. BEEHAVE: a systems model of honeybee colony dynamics and foraging to explore multifactorial causes of colony failure. J. Appl. Ecol. 51, 470–482.
- Becher, M.A., Twiston-Davies, G., Penny, T.D., et al., 2018. Bumble-BEEHAVE: A systems model for exploring multifactorial causes of bumblebee decline at individual, colony, population and community level (J Beggs, Ed,). J. Appl. Ecol. 351, 14.
- Berenbaum, M.R., 2016. Does the honey bee "risk cup" runneth over? Estimating aggregate exposures for assessing pesticide risks to honey bees in agroecosystems. J. Agric. Food Chem. 64, 13–20.
- Biddinger, D.J., Rajotte, E.G., 2015. Integrated pest and pollinator management-adding a new dimension to an accepted paradigm. Curr. Opin. Insect Sci. 10, 204–209.
- Biesmeijer, J.C., Roberts, S.P.M., Reemer, M., et al., 2006. Parallel declines in pollinators and insect-pollinated plants in Britain and the Netherlands. Science 313, 351–354.
- Blühdorn, I., 2011. The politics of unsustainability: COP15, post-ecologism, and the ecological paradox. Organ. Environ. 24, 34–53.
- Bohnenblust, E.W., Vaudo, A.D., Egan, J.F., Mortensen, D.A., Tooker, J.F., 2016. Effects of the herbicide dicamba on nontarget plants and pollinator visitation. Environ. Toxicol. Chem. 35, 144–151.
- Bonmatin, J.-M., Giorio, C., Girolami, V., et al., 2015. Environmental fate and exposure; neonicotinoids and fipronil. Environ. Sci. Pollut. Res. Int. 22, 35–67.
- Borel, B., 2017. CRISPR, microbes and more are joining the war against crop killers. Nature 543, 302–304.
- Bortolotti, L., Sabatini, A.G., Mutinelli, F., et al., 2009. Spring honey bee losses in Italy. Julius-Kühn-Archiv 148–152.

Botías, C., David, A., Hill, E.M., Goulson, D., 2017. Quantifying exposure of wild bumblebees to mixtures of agrochemicals in agricultural and urban landscapes. Environ. Pollut. 222, 73–82.

Brewer, M.J., Goodell, P.B., 2012. Approaches and incentives to implement integrated pest management that addresses regional and environmental issues. Annu. Rev. Entomol. 57, 41–59.

Brittain, C.A., Vighi, M., Bommarco, R., Settele, J., Potts, S.G., 2010. Impacts of a pesticide on pollinator species richness at different spatial scales. Basic Appl. Ecol. 11, 106–115.

Brodt, S., Zalom, F., Krebill-Prather, R., et al., 2005. Almond growers rely on pest control advisers for integrated pest management. Calif. Agric. 59, 242–248.

Bryden, J., Gill, R.J., Mitton, R.A.A., Raine, N.E., Jansen, V.A.A., 2013. Chronic sublethal stress causes bee colony failure. Ecol. Lett. 16. 1463–1469.

Budge, G.E., Garthwaite, D., Crowe, A., et al., 2015. Evidence for pollinator cost and farming benefits of neonicotinoid seed coatings on oilseed rape. Sci. Rep. 5, 12574.

- Cahill Jr., J.F., Elle, E., Smith, G.R., Shore, B.H., 2008. Disruption of a belowground mutualism alters interactions between plants and their floral visitors. Ecology 89, 1791–1801.
- Caro, T.M., O'Doherty, G., 1999. On the use of surrogate species in conservation biology. Conserv. Biol. 13, 805–814.
- Castle, S.J., Goodell, P.B., Palumbo, J.C., 2009. Implementing principles of the integrated control concept 50 years later—current challenges in IPM for arthropod pests. Pest Manag. Sci. 65, 1263–1264.
- Ceballos, G., Ehrlich, P.R., 2018. The misunderstood sixth mass extinction. Science 360, 1080–1081.
- Chaffey, C.E.A., Dobozy, V.A., 2004. Regulation under NAFTA. Pesticide Toxicology and International Regulation, pp. 513–525.
- Ciarlo, T.J., Mullin, C.A., Frazier, J.L., Schmehl, D.R., 2012. Learning impairment in honey bees caused by agricultural spray adjuvants. PLoS One 7, e40848.

Clapp, J., 2017. Bigger is not Always Better: the Drivers and Implications of the Recent Agribusiness Megamergers. University of Waterloo, Waterloo, ON, Canada.

- Clark, M.S., Ferris, H., Klonsky, K., et al., 1998. Agronomic, economic, and environmental comparison of pest management in conventional and alternative tomato and corn systems in northern California. Agric. Ecosyst. Environ. 68, 51–71.
- Couvillon, M.J., Schürch, R., Ratnieks, F.L.W., 2014. Waggle dance distances as integrative indicators of seasonal foraging challenges. PLoS One 9, e93495.
- Cresswell, J.E., 2017. A demographic approach to evaluating the impact of stressors on bumble bee colonies. Ecol. Entomol. 42, 221–229.
- Crone, E.E., Williams, N.M., 2016. Bumble bee colony dynamics: quantifying the importance of land use and floral resources for colony growth and queen production. Ecol. Lett. 19, 460–468.
- Dai, P., Yan, Z., Ma, S., et al., 2018. The herbicide glyphosate negatively affects midgut bacterial communities and survival of honey bee during larvae reared in vitro. J. Agric. Food Chem. 66, 7786–7793.
- Desneux, N., Decourtye, A., Delpuech, J.-M., 2006. The sublethal effects of pesticides on beneficial arthropods. Annu. Rev. Entomol. 52, 81–106.
- Devine, G.J., Furlong, M.J., 2007. Insecticide use: contexts and ecological consequences. Agric. Hum. Values 24, 281–306.
- Di Prisco, G., Cavaliere, V., Annoscia, D., et al., 2013. Neonicotinoid clothianidin adversely affects insect immunity and promotes replication of a viral pathogen in honey bees. Proc. Natl. Acad. Sci. U. S. A. 110, 18466–18471.
- Douglas, M.R., Tooker, J.F., 2015. Large-scale deployment of seed treatments has driven rapid increase in use of neonicotinoid insecticides and preemptive pest management in US field crops. Environ. Sci. Technol. 49, 5088–5097.
- Epstein, L., Bassein, S., 2003. Patterns of pesticide use in California and the implications for strategies for reduction of pesticides. Annu. Rev. Phytopathol. 41, 351–375.
- Epstein, L., Zhang, M., 2014. The impact of integrated pest management programs on pesticide use in California, USA. In: Peshin, R., Pimentel, D. (Eds.), Integrated Pest Management: Experiences with Implementation. Global Overview vol. 4. Springer Netherlands, Dordrecht, pp. 173–200.
- European Commission, 2013. Commission Implementing Regulation (EU) No 485/2013 of 24 May 2013 Amending Implementing Regulation (EU) No 540/2011, as Regards the Conditions of Approval of the Active Substances Clothianidin, Thiamethoxam and Imidacloprid, and Prohibiting the use and Sale of Seeds Treated with Plant Protection Products Containing those Active Substances.
- European Commission, 2017. Report from the Commission to the European Parliament and the Council on the Implementation of Regulation (EC) No 1185/2009 of the European Parliament and of the Council of 25 November 2009 Concerning Statistics on Pesticides.
- 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.
- European Food Safety Authority, 2018. Evaluation of the Data on Clothianidin, Imidacloprid and Thiamethoxam for the Updated Risk Assessment to Bees for Seed Treatments and Granules in the EU.
- Fagerstone, K.A., Bullard, R.W., Ramey, C.A., 1990. Politics and Economics of Maintaining Pesticide Registrations.
- Farrar, J.J., Baur, M.E., Elliott, S.F., 2016. Adoption of IPM practices in grape, tree fruit, and nut production in the Western United States. J. Integr. Pest Manag. Rev. 7.
- Feltham, H., Park, K., Goulson, D., 2014. Field realistic doses of pesticide imidacloprid reduce bumblebee pollen foraging efficiency. Ecotoxicology 23, 317–323.
- Ferrier, P.M., Rucker, R.R., Thurman, W.N., Burgett, M., 2018. Economic Effects and Responses to Changes in Honey Bee Health. US Department of Agriculture.
- Fine, J.D., Cox-Foster, D.L., Mullin, C.A., 2017. An inert pesticide adjuvant synergizes viral pathogenicity and mortality in honey bee larvae. Sci. Rep. 7, 40499.
- Fishel, F.M., Ellis, J., Mc Avoy, G., 2017. Pesticide Labeling: Protection of Pollinators1 (UF/ IFAS Extension).

- Flint, M.L., 2003. Residential pesticide use in California: a report of surveys taken in the Sacramento (Arcade Creek). Stockton (Five-Mile Slough) and San Francisco Bay Areas with Comparisons to the San Diego Creek Watershed of Orange County California.
- Flury, M., 1996. Experimental evidence of transport of pesticides through field soils—a review. J. Environ. Qual. 25, 25–45.
- Fontaine, C., Collin, C.L., Dajoz, I., 2008. Generalist foraging of pollinators: diet expansion at high density. J. Ecol. 96, 1002–1010.
- Forster, R., 2009. Bee poisoning caused by insecticidal seed treatment of maize in Germany in 2008. Julius-Kühn-Archiv 423.
- Freemark, K., Boutin, C., 1995. Impacts of agricultural herbicide use on terrestrial wildlife in temperate landscapes: a review with special reference to North America. Agric. Ecosyst. Environ. 52, 67–91.
- Friedmann, H., 1982. The political economy of food: the rise and fall of the postwar international food order. Am. J. Sociol. 88, S248–S286.
- Funtowicz, S.O., Ravetz, J.R., 1993. Science for the post-normal age. Futures 25, 739–755. Garthwaite, D., Parrish, G., Couch, V., 2018. Amenity Pesticide Usage in the United Kingdom 2016 (Fera)
- Gent, D.H., Mahaffee, W.F., McRoberts, N., Pfender, W.F., 2013. The use and role of predictive systems in disease management. Annu. Rev. Phytopathol. 51, 267–289.
- Gill, R.J., Ramos-Rodriguez, O., Raine, N.E., 2012. Combined pesticide exposure severely affects individual- and colony-level traits in bees. Nature 491, 105–108.
- Girolami, V., Marzaro, M., Vivan, L., et al., 2012. Fatal powdering of bees in flight with particulates of neonicotinoids seed coating and humidity implication. J. Appl. Entomol. 136, 17–26.
- Godfray, H.C.J., Blacquière, T., Field, L.M., et al., 2014. A restatement of the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. Proc. Biol. Sci. 281.
- Godfray, H.C.J., Blacquière, T., Field, L.M., et al., 2015. A restatement of recent advances in the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. Proc. Biol. Sci. 282, 20151821.
- Goldberger, J.R., Lehrer, N., Brunner, J.F., 2013. Adoption of organophosphate alternatives in Washington apple IPM programs: survey evidence from pest management consultants and growers. J. Integr. Pest Manag. Rev. 4, E1–E8.
- 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.
- Government of Ontario, 2016. Ontario's Pollinator Health Action Plan.
- Greatti, M., Sabatini, A.G., Barbattini, R., Rossi, S., Stravisi, A., 2003. Risk of environmental contamination by the active ingredient imidacloprid used for corn seed dressing. Preliminary results. Bull. Insectology 69–72.
- Greene, C., Ferreira, G., Carlson, A., Cooke, B., Hitaj, C., 2017. Growing Organic Demand Provides High-value Opportunities for Many Types of Producers (Amber Waves).
- Greenleaf, S.S., Williams, N.M., Winfree, R., Kremen, C., 2007. Bee foraging ranges and their relationship to body size. Oecologia 153, 589–596.
- Grogan, K.A., Goodhue, R.E., 2012. Spatial externalities of pest control decisions in the California citrus industry. J. Agric. Resour. Econ. 37, 156–179.
- Guarino, B., 2016. "Like it's been nuked": millions of bees dead after South Carolina sprays for Zika mosquitoes. The Washington Post.
- Guha, N., Ward, M.H., Gunier, R., et al., 2013. Characterization of residential pesticide use and chemical formulations through self-report and household inventory: the northern California childhood leukemia study. Environ. Health Perspect. 121, 276–282.
- Hallmann, C.A., Sorg, M., Jongejans, E., et al., 2017. More than 75 percent decline over 27 years in total flying insect biomass in protected areas. PLoS One 12, e0185809.
- Hay, S.I., Guerra, C.A., Tatem, A.J., Noor, A.M., Snow, R.W., 2004. The global distribution and population at risk of malaria: past, present, and future. Lancet Infect. Dis. 4, 327–336.
- Health Canada, 2013. Evaluation of Canadian bee mortalities that coincided with corn planting in spring 2012. Health Canada.
- Helmer, S.H., Kerbaol, A., Aras, P., Jumarie, C., Boily, M., 2015. Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (Apis mellifera). Environ. Sci. Pollut. Res. Int. 22, 8010–8021.
- Henry, M., Cerrutti, N., Aupinel, P., et al., 2015. Reconciling laboratory and field assessments of neonicotinoid toxicity to honeybees. Proc. Biol. Sci. 282.
- Henry, M., Becher, M.A., Osborne, J.L., et al., 2017. Predictive systems models can help elucidate bee declines driven by multiple combined stressors. Apidologie 48, 328–339. Herbert, L.T., Vázquez, D.E., Arenas, A., Farina, W.M., 2014. Effects of field-realistic doses of
- glyphosate on honeybee appetitive behaviour. J. Exp. Biol. 217, 3457–3464.
- Hladik, M.L., Vandever, M., Smalling, K.L., 2016. Exposure of native bees foraging in an agricultural landscape to current-use pesticides. Sci. Total Environ. 542, 469–477.
- Hokkanen, H.M.T., 2015. Integrated pest management at the crossroads: science, politics, or business (as usual)? Arthropod Plant Interact, 9, 543–545.
- Hopwood, J., Code, A., Vaughan, M., et al., 2016. How neonicotinoids can kill bees: the science behind the role these insecticides play in harming bees. Xerces Society.
 Hummel, H.E., Bertossa, M., Hein, D.F., et al., 2005. The western corn rootworm
- Hummel, H.E., Bertossa, M., Hein, D.F., et al., 2005. The western corn rootworm diabrotica Virgifera virgifera en route to Germany. Commun. Agric. Appl. Biol. Sci. 70, 677–686.
- Hussey, D.J., Bell, G.M., 2004. Regulation of pesticides and biocides in the European Union. Pesticide Toxicology and International Regulation, pp. 499–512.
- Hutchison, W.D., Burkness, E.C., Mitchell, P.D., et al., 2010. Areawide suppression of European corn borer with Bt maize reaps savings to non-Bt maize growers. Science 330, 222–225.
- Iwasa, T., Motoyama, N., Ambrose, J.T., Roe, R.M., 2004. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, Apis mellifera. Crop Prot. 23, 371–378.
- Jas, N., 2007. Public health and pesticide regulation in France before and after silent spring. Hist. Technol. 23, 369–388.

Johnson, R.M., Dahlgren, L., Siegfried, B.D., Ellis, M.D., 2013. Acaricide, fungicide and drug interactions in honey bees (Apis mellifera). PLoS One 8, e54092.

Kogan, M., 1998. Integrated pest management: historical perspectives and contemporary developments. Annu. Rev. Entomol. 43, 243–270.

- Kopit, A.M., Pitts-Singer, T.L., 2018. Routes of pesticide exposure in solitary, cavity-nesting bees. Environ. Entomol. 47 (3), 499–510. https://doi.org/10.1093/ee/nvy034.
- Krupke, C.H., Long, E.Y., 2015. Intersections between neonicotinoid seed treatments and honey bees. Curr. Opin. Insect Sci. 10, 8–13.
- 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.
- Ladurner, E., Bosch, J., Kemp, W.P., Maini, S., 2005. Assessing delayed and acute toxicity of five formulated fungicides to Osmia lignaria Say and Apis mellifera. Apidologie 36, 449–460.
- Lebuhn, G., Droege, S., Connor, E.F., et al., 2013. Detecting insect pollinator declines on regional and global scales. Conserv. Biol. 27, 113–120.
 Lichtenberg, E., Zimmerman, R., 1999. Information and farmers' attitudes about pesti-
- Lichtenberg, E., Zimmerman, R., 1999. Information and farmers' attitudes about pesticides, water quality, and related environmental effects. Agric. Ecosyst. Environ. 73, 227–236.
- Lindenmayer, D.B., Likens, G.E., 2010. The science and application of ecological monitoring. Biol. Conserv. 143, 1317–1328.
- Long, E.Y., Krupke, C.H., 2016. Non-cultivated plants present a season-long route of pesticide exposure for honey bees. Nat. Commun. 7, 11629.
- Loos, M., Schipper, A.M., Schlink, U., Strebel, K., Ragas, A.M.J., 2010. Receptor-oriented approaches in wildlife and human exposure modelling: a comparative study. Environ. Model. Softw. 25, 369–382.
- Lundin, O., Smith, H.G., Rundlöf, M., Bommarco, R., 2013. When ecosystem services interact: crop pollination benefits depend on the level of pest control. Proc. Biol. Sci. 280, 20122243.
- Magkos, F., Arvaniti, F., Zampelas, A., 2006. Organic food: buying more safety or just peace of mind? A critical review of the literature. CRC Crit. Rev. Food Sci. Nutr. 46, 23–56. https://doi.org/10.1080/10408690490911846.
- Mauro, I.J., McLachlan, S.M., 2008. Farmer knowledge and risk analysis: postrelease evaluation of herbicide-tolerant canola in Western Canada. Risk Anal. 28, 463–476.
- Meehan, T.D., Gratton, C., 2016. A landscape view of agricultural insecticide use across the conterminous US from 1997 through 2012. PLoS One 11, e0166724.
- Melathopoulos, A., Sagili, R., 2016. Pollinator protection in Oregon. Bee World 93, 104–127.
- Melathopoulos, A.P., Stoner, A.M., 2015. Critique and transformation: on the hypothetical nature of ecosystem service value and its neo-Marxist, liberal and pragmatist criticisms. Ecol. Econ. 117, 173–181.
- Melathopoulos, A.P., Tyedmers, P., Cutler, G.C., 2014. Contextualising pollination benefits: effect of insecticide and fungicide use on fruit set and weight from bee pollination in lowbush blueberry. Ann. Appl. Biol. 165, 387–394.
- Meléndez Ramírez, V., Ayala, R., Delfín González, H., 2018. Crop pollination by stingless bees. In: Vit, P., Pedro, S.R.M., Roubik, D.W. (Eds.), Pot-pollen in Stingless Bee Melittology. Springer International Publishing, Cham, pp. 139–153.
- Michener, C.D., 1969. Comparative social behavior of bees. Annu. Rev. Entomol. 14, 299–342.
- Michener, C.D., 2000. The Bees of the World. JHU Press.
- Moffett, J.O., Morton, H.L., Macdonald, R.H., 1972. Toxicity of some herbicidal sprays to honey bees. J. Econ. Entomol. 65, 32–36.
- Mommaerts, V., Reynders, S., Boulet, J., et al., 2010. Risk assessment for side-effects of neonicotinoids against bumblebees with and without impairing foraging behavior. Ecotoxicology 19, 207–215.
- Morton, H.L., Moffett, J.O., 1972. Ovicidal and larvicidal effects of certain herbicides on honey bees. Environ. Entomol. 1, 611–614.
- Motta, E.V.S., Raymann, K., Moran, N.A., 2018. Glyphosate perturbs the gut microbiota of honey bees. Proc. Natl. Acad. Sci. U. S. A. 115, 10305–10310.
- Mullin, CA., 2015. Effects of "inactive"ingredients on bees. Curr. Opin. Insect Sci. 10, 194–200.
- Mullin, C.A., Frazier, M., Frazier, J.L., et al., 2010. High levels of miticides and agrochemicals in north American apiaries: implications for honey bee health. PLoS One 5, e9754.
- Mussen, E.C., Lopez, J.E., Peng, C.Y.S., 2004. Effects of selected fungicides on growth and development of larval honey bees, Apis mellifera L. (Hymenoptera: Apidae). Environ. Entomol. 33, 1151–1154.
- Neumann, P., Carreck, N.L., 2010. Honey bee colony losses. J. Apic. Res. 49, 1-6.
- Nikolakis, A., Chapple, A., Friessleben, R., et al., 2009. An effective risk management approach to prevent bee damage due to the emission of abraded seed treatment particles during sowing of seeds treated with bee toxic insecticides. Julius-Kühn-Archiv 132.
- Normative Instruction 2, 2017. Brazilian Institute of Environment and Renewable Natural Resources.
- Norris, R.F., Caswell-Chen, E.P., Kogan, M., 2003. Concepts in Integrated Pest Management. Prentice Hall.
- Oerke, E.-C., 2006. Crop losses to pests. J. Agric. Sci. 144, 31-43.
- Oerke, E.-C., Dehne, H.-W., 2004. Safeguarding production—losses in major crops and the role of crop protection. Crop Prot. 23, 275–285.
- Ollerton, J., 2017. Pollinator diversity: distribution, ecological function, and conservation. Annu. Rev. Ecol. Evol. Syst. 48, 353–376.
- Ollerton, J., Winfree, R., Tarrant, S., 2011. How many flowering plants are pollinated by animals? Oikos 120, 321–326.
- Oregon Department of Agriculture, 2015. Permanent Rule Prohibiting the use of Dinotefuran, Imidacloprid, Thiamethoxam, and Clothianidin on Linden Trees.
- Osteen, C.D., Fernandez-Cornejo, J., 2013. Economic and policy issues of U.S. agricultural pesticide use trends. Pest Manag. Sci. 69, 1001–1025.

- Overmyer, J., Feken, M., Ruddle, N., et al., 2018. Thiamethoxam honey bee colony feeding study: linking effects at the level of the individual to those at the colony level. Environ. Toxicol. Chem. 37, 816–828.
- Pardey, P.G., Alston, J.M., Chan-Kang, C., 2013. Public Food and Agricultural Research in the United States: the Rise and Decline of Public Investments, and Policies for Renewal. AGree, Washington, DC.
- Park, M.G., Blitzer, E.J., Gibbs, J., Losey, J.E., Danforth, B.N., 2015. Negative effects of pesticides on wild bee communities can be buffered by landscape context. Proc. Biol. Sci. 282, 20150299.
- Park, M.G., Joshi, N.K., Rajotte, E.G., et al., 2018. Apple grower pollination practices and perceptions of alternative pollinators in New York and Pennsylvania. Renewable Agric. Food Syst. 1–14.
- Pastorok, R.A., Butcher, M.K., Nielsen, R.D., 1996. Modeling wildlife exposure to toxic chemicals: trends and recent advances. Hum. Ecol. Risk. Assess. 2, 444–480.
- Pelaez, V., da Silva, L.R., Araújo, E.B., 2013. Regulation of Pesticides: a Comparative Analysis. Science & Public Policy.
- Pennsylvania Pollinator Protection Plan Task Force, 2017. Pennsylvania Pollinator Protection Plan.
- Perry, C.J., Søvik, E., Myerscough, M.R., Barron, A.B., 2015. Rapid behavioral maturation accelerates failure of stressed honey bee colonies. Proc. Natl. Acad. Sci. U. S. A. 112, 3427–3432.
- Phillips McDougall, 2016. The cost of new agrochemical product discovery, development and registration in 1995, 2000, 2005–8 and 2010–2014. R&D Expenditure in 2014 and Expectations for 2019.
- Phillips McDougall Ltd, 2013. R&D trends for chemical crop protection products and the position of the European market. A Consultancy Study Undertaken for ECPA. Phillips McDougall Ltd.
- Phillips McDougall Ltd, 2016. Agrochemical Research and Development: A Consultancy Study for Crop Life America and the European Crop Protection Association. Phillips McDougall Ltd.
- Pilling, E.D., Bromleychallenor, K.A.C., Walker, C.H., Jepson, P.C., 1995. Mechanism of synergism between the pyrethroid insecticide λ-cyhalothrin and the imidazole fungicide prochloraz, in the honeybee (Apis mellifera L.). Pestic. Biochem. Physiol. 51, 1–11.
- Pimentel, D., Kirby, C., Shroff, A., 1993. The relationship between "cosmetic standards" for foods and pesticide use. In: Pimentel, D., Lehman, H. (Eds.), The Pesticide Question: Environment, Economics, and Ethics. Springer US, Boston, MA, pp. 85–105.
- Pistorius, J., Bischoff, G., Heimbach, U., Stähler, M., 2008. Bee Poisoning Incidents in Germany in Spring 2008 Caused by Abrasion of Active Substance from Treated Seeds During Sowing of Maize. p. 423.
- Pistorius, J., Bischoff, G., Heimbach, U., Stähler, M., 2009. Bee poisoning incidents in Germany in Spring 2008 caused by abrasion of active substance from treated seeds during sowing of maize. Julius-Kühn-Archiv 118.
- Poquet, Y., Vidau, C., Alaux, C., 2016. Modulation of pesticide response in honeybees. Apidologie 47, 412–426.
- Rohr, J.R., Salice, C.J., Nisbet, R.M., 2016. The pros and cons of ecological risk assessment based on data from different levels of biological organization. Crit. Rev. Toxicol. 46, 756–784.
- Rortais, A., Arnold, G., Dorne, J.-L., 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. 587–588, 524–537.
- Ross, K.G., Matthews, R.W., 1991. The Social Biology of Wasps. Cornell University Press.
- Rumkee, J.C.O., Becher, M.A., Thorbek, P., Kennedy, P.J., Osborne, J.L., 2015. Predicting honeybee Colony failure: using the BEEHAVE model to simulate Colony responses to pesticides. Environ. Sci. Technol. 49, 12879–12887.
- Rundlöf, M., Andersson, G.K.S., Bommarco, R., et al., 2015. Seed coating with a neonicotinoid insecticide negatively affects wild bees. Nature 521, 77–80.
- Russell, D., 2004. Integrated pest management for insect pests of cotton in less developed countries. In: Horowitz, A.R., Ishaaya, I. (Eds.), Insect Pest Management: Field and Protected Crops. Springer Berlin Heidelberg, Berlin, Heidelberg, pp. 141–179.
- Samnegård, U., Alins, G., Boreux, V., et al., 2018. Management trade-offs on ecosystem services in apple orchards across Europe: direct and indirect effects of organic production (J Firn, Ed,). J. Appl. Ecol. 46, 528.
- Sánchez-Bayo, F., Goulson, D., Pennacchio, F., et al., 2016. Are bee diseases linked to pesticides? - a brief review. Environ. Int. 89-90, 7–11.
- Schimmelpfennig, D.E., Pray, C.E., Brennan, M.F., 2004. The impact of seed industry concentration on innovation: a study of US biotech market leaders. Agric. Econ. 30, 157–167.
- Schmickl, T., Karsai, I., 2017. Resilience of honeybee colonies via common stomach: a model of self-regulation of foraging. PLoS One 12, e0188004.
 Schmid, R.B., Knutson, A., Giles, K.L., McCornack, B.P., 2018. Hessian fly (Diptera:
- Schmid, R.B., Knutson, A., Giles, K.L., McCornack, B.P., 2018. Hessian fly (Diptera: Cecidomyiidae) biology and management in wheat. J. Integr. Pest Manag. Rev. 9.
- Schreinemachers, P., Tipraqsa, P., 2012. Agricultural pesticides and land use intensification in high, middle and low income countries. Food Policy 37, 616–626.
- Sgolastra, F., Medrzycki, P., Bortolotti, L., et al., 2017. Synergistic mortality between a neonicotinoid insecticide and an ergosterol-biosynthesis-inhibiting fungicide in three bee species. Pest Manag. Sci. 73, 1236–1243.
- 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, 3801.
- 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.
- Sparks, T.C., Lorsbach, B.A., 2017. Perspectives on the agrochemical industry and agrochemical discovery. Pest Manag. Sci. 73, 672–677.
- Sponsler, D.B., Johnson, R.M., 2017. Mechanistic modeling of pesticide exposure: the missing keystone of honey bee toxicology. Environ. Toxicol. Chem. 36 (4), 871–881.

- Stanley, D.A., Garratt, M.P.D., Wickens, J.B., et al., 2015. Neonicotinoid pesticide exposure impairs crop pollination services provided by bumblebees. Nature 528, 548–550.
- Stember, M., 1991. Advancing the social sciences through the interdisciplinary enterprise. Soc. Sci. J. 28, 1–14.Stern, V., Smith, R., Van den Bosch, R., Hagen, K., Others, 1959. The integration of chemical
- and biological control of the spotted alfalfa aphid: the integrated control concept. Hilgardia 29, 81–101.
- Stoner, A.M., 2014. Sociobiophysicality and the necessity of critical theory: moving beyond prevailing conceptions of environmental sociology in the USA. Crit. Sociol. 40, 621–642.
- Suryanarayanan, S., 2015. Pesticides and pollinators: a context-sensitive policy approach. Curr. Opin. Insect Sci. 10, 149–155.
- Suryanarayanan, S., Kleinman, D.L., 2014. Beekeepers' collective resistance and the politics of pesticide regulation in France and the United States. Polit. Power Soc. Theory 27, 89–122.
- Tewksbury, J.J., Anderson, J.G.T., Bakker, J.D., et al., 2014. Natural history's place in science and society. Bioscience 64, 300–310.
- The European Commission, 2018a. Commission implementing regulation (EU) 2018/785. Off. J. Eur. Union L 132/40.
- The European Commission, 2018b. Commission implementing regulation (EU) 2018/783. Off. J. Eur. Union L 132/31.
- The European Commission, 2018c. Commission implementing regulation (EU) 2018/784. Off. J. Eur. Union L 132/35.
- Thompson, H.M., Fryday, S.L., Harkin, S., Milner, S., 2014. Potential impacts of synergism in honeybees (Apis mellifera) of exposure to neonicotinoids and sprayed fungicides in crops. Apidologie 45, 545–553.
- Thorbek, P., Campbell, P.J., Sweeney, P.J., Thompson, H.M., 2017. Using BEEHAVE to explore pesticide protection goals for European honeybee (Apis melifera L.) worker losses at different forage qualities. Environ. Toxicol. Chem. 36, 254–264.
- Tooker, J.F., Douglas, M.R., Krupke, C.H., 2017. Neonicotinoid seed treatments: limitations and compatibility with integrated pest management. Agric. Environ. Lett. 2.
- Tsvetkov, N., Samson-Robert, O., Sood, K., et al., 2017. Chronic exposure to neonicotinoids reduces honey bee health near corn crops. Science 356, 1395–1397.
- United States General Accounting Office, 2001. Management Improvements Needed to Further Promote Integrated Pest Management. United States General Accounting Office.
- US Environmental Protection Agency, 2014. Guidance for Assessing Pesticide Risks to Bees.
- US Geological Survey, 2007. The Quality of Our Nation's Waters—Pesticides in the Nation's Streams and Ground Water, 1992–2001.

USDA-NASS, 2018. Quick Stats. National Agricultural Statistics Service, US Department of Agriculture.

- USGCRP, 2018. In: Reidmiller, D.R., Avery, C.W., Easterling, D.R., Kunkel, K.E., Lewis, K.L.M., Maycock, T.K., Stewart, B.C. (Eds.), Impacts, Risks, and Adaptation in the United States: Fourth National Climate Assessment. vol. 2. U.S. Global Change Research Program, Washington, DC. https://doi.org/10.7930/NCA4.2018.
- van der Geest, B., 2012. Bee poisoning incidents in the Pomurje region of eastern Slovenia in 2011. Julius-Kühn-Archiv 124.
- Vázquez, D.E., Ilina, N., Pagano, E.A., Zavala, J.A., Farina, W.M., 2018. Glyphosate affects the larval development of honey bees depending on the susceptibility of colonies. PLoS One 13, e0205074.
- Wechsler, S., Smith, D., 2018. Has resistance taken root in U.S. corn fields? Demand for insect control. Am. J. Agric. Econ. 100, 1136–1150.
- Wilen, C.A., 2001. Survey of Residential Pesticide use and Sales in the San Diego Creek Watershed of Orange County, California. University of California Statewide IPM Project.
- Wilen, C., 2002. Survey of Residential Pesticide use in the Chollas Creek Area of San Diego county and Delhi Channel of Orange County, California. University of California Statewide IPM Project.
- The world of organic agriculture. In: Willer, H., Lernoud, J. (Eds.), Statistics and Emerging Trends 2016. Research Institute of Organic Agriculture (FiBL), Frick, Switzerland, and IFOAM - Organics International, Bonn.
- Willmer, P.G., Cunnold, H., Ballantyne, G., 2017. Insights from measuring pollen deposition: quantifying the pre-eminence of bees as flower visitors and effective pollinators. Arthropod Plant Interact. 1–15.
- Woodcock, B.A., Isaac, N.J.B., Bullock, J.M., et al., 2016. Impacts of neonicotinoid use on long-term population changes in wild bees in England. Nat. Commun. 7, 12459.
- Woodcock, B.A., Bullock, J.M., Shore, R.F., et al., 2017. Country-specific effects of neonicotinoid pesticides on honey bees and wild bees. Science 356, 1393–1395.
- World Health Organization, 2006. Pesticides and their Application: for the Control of Vectors and Pests of Public Health Importance.
- World Health Organization, 2014. The International Code of Conduct on Pesticide Management. FAO.
- Xerces Society, 2013. Pesticide Causes Largest Mass Bumble Bee Death on Record.
- Yang, W.-R., Grieneisen, M., Chen, H., Zhang, M., 2015. Reduction of crop diversity does not drive insecticide use. J. Agric. Sci. 7, 1.
- Zurbuchen, A., Cheesman, S., Klaiber, J., et al., 2010. Long foraging distances impose high costs on offspring production in solitary bees. J. Anim. Ecol. 79, 674–681.