Integrative Zoology 2024; 19: 442–457 doi: 10.1111/1749-4877.12752

REVIEW

INTEGRATIVE ZOOLOGY

Biotic and abiotic stresses on honeybee health

Zheguang LIN, Siyi SHEN, Kang WANG and Ting JI

Apicultural Research Institute, College of Animal Science and Technology, Yangzhou University, Yangzhou, China

Abstract

Honeybees are the most critical pollinators providing key ecosystem services that underpin crop production and sustainable agriculture. Amidst a backdrop of rapid global change, this eusocial insect encounters a succession of stressors during nesting, foraging, and pollination. Ectoparasitic mites, together with vectored viruses, have been recognized as central biotic threats to honeybee health, while the spread of invasive giant hornets and small hive beetles also increasingly threatens colonies worldwide. Cocktails of agrochemicals, including acaricides used for mite treatment, and other pollutants of the environment have been widely documented to affect bee health in various ways. Additionally, expanding urbanization, climate change, and agricultural intensification often result in the destruction or fragmentation of flower-rich bee habitats. The anthropogenic pressures exerted by beekeeping management practices affect the natural selection and evolution of honeybees, and colony translocations facilitate alien species invasion and disease transmission. In this review, the multiple biotic and abiotic threats and their interactions that potentially undermine bee colony health are discussed, while taking into consideration the sensitivity, large foraging area, dense network among related nestmates, and social behaviors of honeybees.

Key words: abiotic stressor, *Apis*, biotic stressor, colony losses, interaction effect, pollinator decline

INTRODUCTION

Pollinators provide an important ecosystem service by playing a key functional role in sustaining both wild plant communities and agricultural productivity (Potts *et al.* 2016). Animal-mediated pollination services benefit over three-quarters of crop plants (Porto *et al.* 2020), and the immense value of insect pollination in improving crop quantity and quality has been widely recognized (Fijen *et al.* 2018; Khalifa *et al.* 2021). Insects, particularly honeybees, are the primary pollinators of both crops and wild plants. However, concerns have been raised that invertebrate pollinator populations, both in the wild and under management, are declining worldwide, particularly in the Northern Hemisphere (Neumann & Carreck 2010; Pirk *et al.* 2016; Ulrich *et al.* 2020; van der Sluijs 2020). Although this argument has been sometimes challenged (e.g. Ghazoul 2005), the dependency of crops on pollinators is undeniably increasing (Aizen *et al.* 2019; Garibaldi *et al.* 2020), and alternatives such as robot bees cannot yet effectively counter pollination deficiency (Potts *et al.* 2018; Gleadow *et al.* 2019). In many parts of the world, reliance on managed pollinators, including the western and eastern honeybees—*Apis mellifera* and *Apis cerana*, respectively, is prevailing owing to the value of their products and their crop pollination efficiency both spatially and in a timely manner. Honeybees live in colonies and visit various flowering plants by foraging, during which they face a variety of biotic and abiotic threats and frequently interact with related nestmates and intercolonial or interspecies individuals (Leong

Correspondence: Ting Ji, College of Animal Science and Technology, Yangzhou University, 88 South University Rd, Yangzhou 225009, China.
Email: tji@yzu.edu.cn

et al. 2016; Quigley *et al.* 2019; Pusceddu *et al.* 2021; Siviter *et al.* 2021). Consequently, colony loss resulting from the aforementioned challenges has emerged as a crucial issue in global apiculture (Steinhauer *et al.* 2018; Hristov *et al.* 2020). In this review, we aimed to comprehensively summarize the multiple biotic and abiotic threats and their interactions that potentially undermine bee colony health to offer insights regarding the studies of honeybee health and to provide guidance to the apiculturists and policymakers.

BIOTIC STRESSORS

Ectoparasitic mites

Two ectoparasitic mite genera, *Varroa* and *Tropilaelaps* with a global and mostly Asian distribution, respectively, inflict insurmountable problems on *A. mellifera* populations (Nazzi & Le Conte 2016; de Guzman *et al.* 2017). Although four species of each *Varroa* and *Tropilaelaps* have been identified, only *Varroa destructor* and *Tropilaelaps mercedesae* are threatening colony health, to an extent that could lead to colony collapse if not for human intervention (Chantawannakul *et al.* 2018; Traynor *et al.* 2020). This is evident from the fact that most wild and aferal populations of *A. mellifera* in the Northern Hemisphere have been eradicated due to the lack of treatment (Kraus & Page 1995; Oldroyd 2007; Strauss *et al.* 2016; Pirk *et al.* 2017).

Varroa destructor feeds exclusively on the host's fat body, consuming nearly a microliter daily (Ramsey *et al.* 2018, 2019; Posada-Florez *et al.* 2019) and significantly interfering with honeybee physiology (Amdam *et al.* 2003; Arrese & Soulages 2010). The life cycle of *V. destructor* consists of two stages, the phoretic dispersal phase, during which it parasitizes adult bees, and the reproductive phase, closely synchronized with the host's development, during which it infests immature individuals (Traynor *et al.* 2020).

Most biological features of *Tropilaelaps* are similar to those of *Varroa* excluding the former's smaller body size, rapid locomotion, faster reproduction rate, and ability to mate outside brood cells (de Guzman *et al.* 2017; Chantawannakul *et al.* 2018; Gao *et al.* 2021). Although *Tropilaelaps* mites are more prevalent than *Varroa* mites in some Asian *A. mellifera* colonies (Buawangpong *et al.* 2015), studies on this parasitic mite are still in their initial stages, and more investigations are needed.

Several behaviors, such as worker auto-grooming, allogrooming, and hygienic behavior (Bąk & Wilde 2015; Locke 2016; Leclercq *et al.* 2017; Nganso *et al.* 2017; Pusceddu *et al.* 2021), have been observed in naturally surviving *A. mellifera* colonies, whereas reduced mite-reproductive success seems to be a primary determinant of mite-resistance (Oddie *et al.* 2017; Nganso *et al.* 2018). Notably, cell recapping was recently evidenced to be associated with lower mite reproductive success (Lin *et al.* 2018; Grindrod & Martin 2021; Oddie *et al.* 2021). Indeed, controlling the reproduction of parasites is key to maintaining the balance of the host–parasite relationship in favor of the host. Therefore, investigating the population dynamics of ectoparasitic mites and their host-finding and reproductive behaviors is vital for controlling these mites in honeybee colony management. Once the directional mechanism of mites is determined, biological approaches, such as pheromones for trapping, repelling, or interfering with their mating behavior, can be used to limit the population growth of these ectoparasites.

A lack of coevolution between ectoparasitic mites and *A. mellifera*, which was first infested a few decades ago (De Jong *et al.* 1982), is considered a key factor in the susceptibility of the honeybee host. Considering the poor efficacy and negative side effects of medication-based approaches (Dietemann *et al.* 2012), breeding efforts are aimed at selecting honeybee stocks that can resist these serious biotic threats worldwide (Büchler *et al.* 2010). The immune mechanism responsible for the defense of bee colonies and for individuals to cope with external threats is characterized by plasticity (Mondet *et al.* 2015), and thus, artificially selecting honeybee stocks (Hopkins *et al.* 2012) for resistance to primary biotic threats is an important form of human intervention to accelerate colony evolution (Lin *et al.* 2023) and achieve resistance. However, relevant studies have made limited progress in recent years due to, in our opinion, knowledge gaps in the relationship between mites and their original hosts. Recent evidence supports that immature *A. cerana* individuals are more susceptible (Page *et al.* 2016; Lin *et al.* 2018, 2022) and its adult workers are significantly more efficient in the rapid detection and removal of dead brood (Lin *et al.* 2016), which is also observed in the mite-resistant *A. mellifera* stocks (Villa *et al.* 2009), limiting the reproduction of parasitic mites (Page *et al.* 2016; Lin *et al.* 2018, 2021a; Wang *et al.* 2020). These characteristics can be informative for *A. mellifera* breeding programs.

Microorganisms

Pathogenic microorganisms play a crucial role in ecosystems (Preston *et al.* 2016; Piot *et al.* 2022). Host pathogen infections can be divided into covert and overt ones, determined by factors such as the coevolution time between the pathogen and host, physiological function of the host, antiviral response, transmission route, and environmental factors (Rigaud *et al.* 2010; Britton & Jane White 2021). In covert infections, the proliferation of pathogens is limited, reducing the probability of the horizontal transmission of pathogens between hosts. However, the long-term survival of infected hosts increases the likelihood of vertical transmission from queens and drones to offspring (Chen *et al.* 2006b). In contrast, overt infections are typically characterized by the rapid replication of the pathogen within an individual, leading to increased virulence and opportunities for horizontal transmission via trophallaxis and shared food resources (Chen *et al.* 2006a).

Owing to the rapid advances in and increasing accessibility of high-throughput sequencing technologies, >60 honeybee-infecting viruses have been identified (Beaurepaire *et al.* 2020), with the most detrimental being mainly single-stranded positive-sense RNA viruses from the families of *Dicistroviridae* and *Iflaviridae*. Viruses from the *Dicistroviridae* family (dicistroviruses) include acute bee paralysis virus, black queen cell virus, Israeli acute paralysis virus, and Kashmir bee virus, whereas *Iflaviridae* viruses (iflaviruses) include deformed wing virus, slow bee paralysis virus, and sacbrood virus, as well as the taxonomically unsystematic chronic bee paralysis virus (Grozinger & Flenniken 2019; Procházková *et al.* 2020; Ullah *et al.* 2021). Sacbrood virus and deformed wing virus, in particular, have attracted the most attention and have been the subject of investigation in *A. cerana* and *A. mellifera* virology, respectively (Gong *et al.* 2016; Beaurepaire *et al.* 2020; Wei *et al.* 2022). The structures of most of these common viruses have been deciphered (Kalynych *et al.* 2017; Škubník *et al.* 2017, 2021; Spurny *et al.* 2017; Procházková *et al.* 2018; Acosta-Reyes *et al.* 2019), aiding the development of antiviral compounds. Both dicistroviruses and iflaviruses are enveloped in capsids with icosahedral symmetries, while iflavirus genome release is facilitated by a large opening of the viral capsid and triggered by an acidic pH, which is typical in endosomes, indicating that the viruses may enter cells by endocytosis (Procházková *et al.* 2020; Škubník *et al.* 2021). However, our understanding of honeybee virology at the molecular level is limited because of a lack of stable honeybee tissue cell lines (Guo *et al.* 2020).

Similar to other organisms, bee viruses affect various aspects of honeybee biology and cause a variety of well-recognized effects, such as body malformation, stunted development, tremor paralysis, decreased immunity, diminished reproductive capability, impaired cognition and homing ability, navigation system loss, and shortened life span (McMenamin & Flenniken 2018; reviewed by Ullah *et al.* 2021). The spread and virulence of viruses can be largely facilitated by ectoparasitic mites (discussed in the section of Interactive and cumulative effects of multiple stressors).

In addition to viruses, bacterial (e.g. *Paenibacillus larvae* and *Melissococcus plutonius*) and fungal (e.g. *Nosema ceranae*) pathogens threaten honeybee health. *Paenibacillus larvae* and *M. plutonius*, the causative agents of American foulbrood and European foulbrood, mainly infect the larvae of *A. mellifera* and *A. cerana*, respectively, consequently leading to the collapse of a colony if left untreated (Alonso-Salces *et al.* 2017; de León-Door *et al.* 2020; Devi *et al.* 2021). Although the absence of antibodies in insects leads to a deficiency in transgenerational immunity, the survival rate of the offspring of orally vaccinated queens can be largely increased after *P. larvae* challenge (Dickel *et al.* 2022). *Nosema ceranae* is an obligate intracellular eukaryotic parasite that affects adult bees and has been intensively studied over the past dozen years since its first detection. It was extensively detected coincidentally in collapsing colonies after infection similar to the outbreak of Colony Collapse Disorder scenario in the United States (Chen *et al.* 2008; Higes *et al.* 2008; Martín-Hernández *et al.* 2018). *Nosema ceranae* invades the midgut and affects different castes of several bee species (Goulson *et al.* 2015) in terms of physiological processes, behavioral performance, metabolism, immune response, and so on (Paris *et al.* 2018; reviewed by Martín-Hernández *et al.* 2018).

Large biotic enemies

Honeybees face numerous biotic enemies during nest-living and foraging activities, such as the predatory hornet, wax moth, mantis, Batrachia, and small hive beetle. The giant hornet *Vespa*, causing honeybee foragers homing failure and colony foraging paralysis, is native to Asia and invaded Europe and America during this century (Requier *et al.* 2019; Zhu *et al.* 2020; Werenkraut *et al.* 2022). This predator hunts arthropods, including *A. cerana* and *A. mellifera*, for food and decreases the survival probability of colonies of the latter due to a lack of effective defenses (Tan *et al.* 2007; Requier *et al.* 2019).

The small hive beetle (*Aethina tumida*), feeding on both fruits and bee nest products, originated in sub-Saharan Africa and is now distributed almost globally (Evans *et al.* 2018), which may partially be facilitated by the international beeswax trade (Idrissou *et al.* 2019). At present, our limited knowledge of its biology, diagnosis, control, and prevention restricts the development of efficient treatments (reviewed by Neumann *et al.* 2016), which is also the case for other honeybee pests and diseases. Therefore, maintaining a healthy colony via good beekeeping management is commonly the ideal approach for disease prevention.

ABIOTIC STRESSORS

Agrochemicals

In modern agricultural systems, pollinators are readily exposed to agrochemicals during periods that they heavily rely on blooming crops. Honeybees can be utilized as bioindicators of the effects of agrochemicals and land-use on pollinators in view of their sensitivity and ability to provide high-resolution information regarding the presence of environmentally persistent agrochemicals and to reflect changes in agricultural landscape quality at spatial and temporal scales (Quigley *et al.* 2019). Mounting evidence suggests that agrochemicals, including pesticides, fungicides, herbicides, and acaricides, are one of the most direct and severe threats to honeybee physiology and colony health, and some of them, particularly neonicotinoids, have been directly implicated in colony collapse (Goulson *et al.* 2015; Sánchez-Bayo *et al.* 2016; Siviter *et al.* 2021; Wang *et al.* 2021a). Numerous types of extremely toxic agrochemicals that directly cause acute toxicity and lethality to pollinators are banned or restricted in agricultural practices in several countries. However, the sublethal negative effects of medium- or low-toxicity agrochemicals, partially due to their prophylactic use in the surroundings, can still disrupt the physiology and behavior of all caste bees in the hive.

The reproductive toxicity of agrochemicals to queens and drones has always been in focus as it dramatically affects colony growth and sustainability. Even in cases of high mating frequencies, neonicotinoid-exposed queens may have compromised ovaries and spermathecal-stored sperm quality and quantity, adversely affecting reproduction (Rangel & Tarpy 2015; Williams *et al.* 2015). Physiological disorders in the queens, such as decreased attractiveness of pheromones to workers (Walsh *et al.* 2020) and dysfunctional gene expression related to antioxidant, immunity, and development, lead to reduced control of the colony (Chaimanee *et al.* 2016; Costa *et al.* 2022). Agrochemicals can significantly affect the quality and viability of drones and their sperm (Straub *et al.* 2016). Deltamethrin, acetamiprid, fumagillin, thiamethoxam, clothianidin, and fipronil exposure reduces drone survival and sperm viability and concentration and increases the percentage of sperm with defective membrane integrity while increasing sperm metabolism, which may be associated with drone infertility (Kairo *et al.* 2016; Fisher & Rangel 2018; Ben Abdelkader *et al.* 2021; Straub *et al.* 2021). These stresses on queens and drones undermine sustainability, directly resulting in the loss of workers and causing colony collapse.

Worker bees constitute the largest part of the population and undertake almost all labor in hives. Compared with queens and drones, worker bees are more likely to be exposed to agrochemicals because of their foraging activities. The transfer of agrochemical residues in the hive compartments to the honeybee brood, augmented in both variety and dose, is inevitable (Morales *et al.* 2020). In addition to acute toxicity and death (Raymann *et al.* 2018; Tihelka 2018), sublethal effects of agrochemicals on brood development, including delayed larval development and reduced adult hatching weight, have been observed (Wu *et al.* 2011; Odemer *et al.* 2020), especially under high hive temperatures where the sublethal effects are exacerbated (Medrzycki *et al.* 2010; Wu *et al.* 2011). The dysfunctional development of the neural tissues caused by neurotoxic substances has been extensively investigated in honeybees (Desneux *et al.* 2007). Neonicotinoids have been shown to impair learning and memory in honeybees, directly affecting the ability of workers to navigate and forage (Tan *et al.* 2017; Muth & Leonard 2019; Muth *et al.* 2019). Consequently, workers appear disoriented, have a degenerated sucrose responsiveness (Eiri & Nieh 2012; DÈmares *et al.* 2016), consume less food (Wang *et al.* 2022), and require more time to discern food. These physiological changes may explain why workers exhibit decreased waggle dancing and foraging success after neonicotinoid exposure (Eiri & Nieh 2012; Henry *et al.* 2012; Teeters *et al.* 2012). Additionally, agrochemicals have the potential to disrupt gut microbes (Kakumanu *et al.* 2016; Paris *et al.* 2020; Wang *et al.* 2023) and increase susceptibility to infection by opportunistic pathogens (Motta *et al.* 2018).

Environmental change

A decreased pathogenicity of common pathogens in the wild non-cave *Apis* spp. (Lin *et al.* 2021b) indicates the potential role of environmental change in the observed decline of pollinators. Amidst the backdrop of global change reflected by climate change, expanding urbanization, and agricultural intensification, pollinator biodiversity and flower-rich habitats are being destroyed or fragmented (Potts *et al.* 2016; Goulson & Nicholls 2022). Climate change affects flora and fauna and their interactions, including flowering phenology, floral rewards, honeybee behavior, and plant pollinator interactions, resulting in novel communities and altered ecosystems (Keeler *et al.* 2021; Vercelli *et al.* 2021). Extreme temperatures and reduced precipitation can end flower blooms prematurely, accelerate the wilting of flowers, and reduce pollen and nectar availability (Flores *et al.* 2019; Sayğı 2020), affecting the symbiosis of honeybees and flowering plants that they pollinate, given that time and pattern of flowering, as well as pollinating activity, are sensitive to temperature (Hegland *et al.* 2009; Forrest 2015). The prolificity of queens, spermatogenesis of drones, and viability of honeybee broods can also be negatively influenced by high atmospheric temperatures, leading to a reduction in the reproductive function of queens and thermoregulation of worker bees, and thus to colony homeostasis disruption (Sales *et al.* 2018; Cebotari *et al.* 2019; Walsh *et al.* 2019; McAfee *et al.* 2020; Cunningham *et al.* 2022).

Urbanization and land-use intensity can lead to the loss of natural habitats for bees and thus to decreased abundance of floral resources and nesting opportunities, resulting in a reduction in the number, richness, and diversity of bees (Jaffé *et al.* 2019; Millard *et al.* 2021). A decline in brood emergence occurs when honeybees are unable to adapt or find new habitats, affecting colony continuation (McCabe *et al.* 2022). Although urbanization can increase the abundance of floral resources to a certain extent, which would benefit some honeybee populations and partially compensate for its negative effects, this is often limited by urban warming and the loss of agricultural land (Wilson & Jamieson 2019). The expanse of industrial agriculture has intensely modified the landscape across large areas of the world, often reducing the availability and diversity of floral resources (Goulson & Nicholls 2022). As a result of agricultural intensification practices, such as large-scale cultivation, monoculture, and highly disturbed agronomic practices, the biodiversity of pollinating insects in and around fields has been decreased (Marshman *et al.* 2019; Seibold *et al.* 2019; Raven & Wagner 2021). Overall, the impact of environmental change can be determined by studying the accessibility of floral resources and the functional characteristics of honeybee populations.

Environmental pollutants

Honeybees interact with air, soil, water, and utilitarian plants during flight and foraging and are directly exposed to various environmental pollutants, such as microplastics, heavy metals, and particulate matter (PM). Vast quantities of pollutants have been detected in different tissues of pollinators (Feldhaar & Otti 2020; Deng *et al.* 2021; Edo *et al.* 2021). Honeybees are, therefore, generally used as sentinel bioindicators in environmental monitoring plans due to their sensitivity, large foraging area, morphological features, and social behaviors (Bargańska *et al.* 2016; Herrero-Latorre *et al.* 2017; Goretti *et al.* 2020; Gutiérrez *et al.* 2020; Capitani *et al.* 2021). Honeybees could also serve as bioindicators of environmental SARS-CoV-2 prevalence, since coronavirus particles have widely been detected in the PM carried by foraging workers (Cilia *et al.* 2022). In addition, as honeybees distribute environmental pollutants within the colony during food transfer, the risks of environmental pollutants present in bee products to human health also need to be considered (Diaz-Basantes *et al.* 2020; Papa *et al.* 2021; Smith & Weis 2022).

The large-scale use of plastic has contributed to huge quantities of hazardous refuse being produced at a global level and represents one of the most prominent issues of the Anthropocene (Cox *et al.* 2019; Zhang *et al.* 2020). Microplastics are ubiquitous and persistent in almost all environments and pose a potential threat to a variety of plant and animal species (Anbumani & Kakkar 2018; Mammo *et al.* 2020). Exposure to microplastics will commonly not lead to acute mortality of honeybees in the short term; rather, it decreases the gut microbiome diversity, alters the microbiome structure, and changes the expression of genes related to detoxification and immunity (Wang *et al.* 2021b; Balzani *et al.* 2022; Buteler *et al.* 2022).

Atmospheric PM, primarily emitted by vehicular transport, combustion engines, coal mining, and agricultural residues, have been demonstrated to affect the navigation of honeybee workers, increasing the foraging duration, and affecting bee survival, flower visitation, heart rate, hemocyte levels, and gene expression (Thimmegowda *et al.* 2020; Cho *et al.* 2021). Coupled with heavy metals, such as lead, copper, and manganese, the exposures exert potential neurotoxic effects, including damage to learning and long-term memory formation through impaired protein functioning, gut lining damage and microbiome alterations, immune system activation, and aberrant DNA methylation, eventually causing lethal or sublethal effects on honeybees (Burden 2016; Costa *et al.* 2019;

Al Naggar *et al.* 2020). Furthermore, noise, turbulence and dust in road verges have been evidenced to impact honeybee forager activities as well (Dargas *et al.* 2016; Phillips *et al.* 2021), although the benefits of road verges to pollinators may outweigh the costs (Phillips *et al.* 2020).

Human management

Lack of natural selection

Although beekeepers play a crucial role in controlling colony diseases, such as regular queen renewal to promote honeybee health (Simeunovic *et al.* 2014), the role of apiculture in limiting natural selection and evolution negatively contributes to colony health (Neumann & Blacquière 2017; Oddie *et al.* 2017). To maintain a productive colony, modern beekeepers perform regular treatments to ensure its survival, which is contrary to the law of natural selection (Le Conte *et al.* 2020). Drug treatments may interfere with the natural population dynamics of colonial endosymbionts (Neumann & Blacquière 2017). In addition, the intensification of colony density by commercial beekeeping increases the probability of drifting foragers, thus facilitating the pathophoresis of infectious diseases (Seeley & Smith 2015).

Interspecific competition and disease transmission after colony translocations

The anthropogenic introduction of domestic species to regions beyond their natural habitat range can lead to competition with endemic creatures and may result in biological invasions affecting living organisms (Young *et al.* 2017). Although there is little evidence that introduced managed honeybees have a major impact on the survival, fecundity, and population density of other pollinators, they most likely have negative effects on other honeybee species (Moritz *et al.* 2005). The high number of introduced *A. mellifera* colonies in Asia could lead to direct competition with endemic cavity-nesting honeybee species (such as *A. cerana*, *Apis koschevnikovi*, *Apis nigrocincta*, and *Apis nuluensis*) for nest sites and with all managed and wild honeybees for floral resources (IPBES 2016; Geslin *et al.* 2017; Mallinger *et al.* 2017; Vanbergen *et al.* 2018). *Apis mellifera* may also interfere with mating of virgin *A. cerana* queens and steal stored honey from native honeybees (Theisen-Jones & Bienefeld 2016).

It is widely recognized that the introduction of alien species can lead to the spread of infectious diseases (Crowl *et al.* 2008; Hulme 2014). Managed honeybee translocations across regions, countries, and continents facilitated by human migration and trade have contributed to ongoing disease transmission as a consequence of colony introduction and communication (Beaurepaire *et al.* 2020). Meanwhile, alien species in a new habitat are more susceptible to diseases than native pollinators, which usually have a survival advantage, as demonstrated by the greater susceptibility of *A. mellifera*, introduced in Southeast Asia, to the invasive ectoparasitic *Varroa* and *Tropilaelaps* mites compared to that of the native *A. cerana* (Nazzi & Le Conte 2016; de Guzman *et al.* 2017; Traynor *et al.* 2020). In this regard, the invasion of alien mites has constrained the establishment of feral *A. mellifera* populations in Asia so far. In other words, ectoparasites can protect wild and managed Asian honeybees, including their original hosts against invasion.

Malnutrition

Adequate nutrition is fundamental to the health of organisms at all life stages (Wickramasinghe *et al.* 2020). Nectar and pollen, the primary nutritional resources collected by honeybees, are rich in carbohydrates, proteins, lipids, and micronutrients (Vaudo *et al.* 2015; Tsuruda *et al.* 2021). Apicultural practices govern colony nutrition through the choice of foraging areas for worker bees (Neumann & Blacquière 2017). However, the increased colony density in modern apiculture leads to high demand for foraging resources. Beekeepers exploiting honeybee colonies for hive products and providing workers with syrup and soybean flour in exchange can compromise colony health and affect its resilience to diseases (Mao *et al.* 2013; Wheeler & Robinson 2014). Evidence emerges that a modest amount of probiotics appears beneficial to the fitness of honeybees (Evans & Lopez 2004; Brown *et al.* 2022), although few studies have investigated the issue despite the key role of the gut microbiota in bee health (Kwong & Moran 2016). Unfortunately, because of the nutritional knowledge gap, a standard balanced diet is currently lacking in commercial beekeeping, highlighting the need for further studies to correct this situation (Paray *et al.* 2021; reviewed by Tsuruda *et al.* 2021).

INTERACTIVE AND CUMULATIVE EFFECTS OF MULTIPLE STRESSORS

Generally, biotic and abiotic stressors do not act independently, and quite often, additive or synergistic effects have been demonstrated to impact colony health (O'Neal *et al.* 2018; Siviter *et al.* 2021; Goulson & Nicholls 2022). Typically, there is a finely balanced relationship between microbial pathogens and their host (Varela *et al.* 2009; Deroost *et al.* 2015). Multiple microbial pathogens can interact with each other to achieve mutual benefit and reciprocity (Gajda *et al.* 2021). However, when the natural dynamic balance is disturbed, the pathogens can inflict devastating effects on their hosts. For example, pathogen virulence can increase with the introduction of a second host when a multi-host pathogen, such as a deformed wing virus vectored by *V. destructor*, spreads among species (Woolhouse *et al.* 2001; Martin *et al.* 2012). *Varroa destructor* can serve as a harbor for virus replication and transmission as a result of bias proliferating highly virulent strains and weakening host immunity (Di Prisco *et al.* 2011; Martin *et al.* 2012; Lin *et al.* 2022). Furthermore, virus-induced immunosuppression in hosts can favor the feeding and reproductive behavior of ectoparasitic mites (Di Prisco *et al.* 2016). On the other hand, the fitness of mites may also be influenced by the vectored viruses, a subject yet to be further investigated (e.g. Wang *et al.* 2019; Ryabov *et al.* 2022).

The decline in honeybee populations has been reported to be associated with nutritional shortage caused by land-use intensification (Vaudo *et al.* 2015). A well-sustained nutritional state not only enhances the survival of pathogen-infected hosts, but also significantly shapes the microsporidian–virus interface (Zheng *et al.* 2014; Tritschler *et al.* 2017). On the contrary, nutritional stress adversely affects honeybee immunity and renders bees more susceptible to microbial pathogens, while vice versa some pathogens have detrimental effects on the nutritional resilience of their hosts (Dolezal & Toth 2018; Grozinger & Flenniken 2019; Castelli *et al.* 2020). Additionally, nutritional stress combined with pesticides can reduce the food consumption of honeybees and their flight success, leading to increased mortality (Tong *et al.* 2019). Regarding other abiotic factors, urbanization increases pathogenic pressure on honeybees, and climate change will increase the risk of hornet and non-native bee species invasions (Barbet-Massin *et al.* 2013; Tabor & Koch 2021) and affect the prevalence of infectious diseases, including viruses, American foulbrood, *N. ceranae*, and small hive beetles (Lindgren *et al.* 2012; Martín-Hernández *et al.* 2018; Cornelissen *et al.* 2019; Jamal *et al.* 2021; de Jongh *et al.* 2022; Piot *et al.* 2022). The ingestion and accumulation of microplastics and antibiotics in honeybees can also undermine their antiviral defenses (Deng *et al.* 2021, 2022). In addition to viruses and *Nosema* (Aufauvre *et al.* 2012; Di Prisco *et al.* 2013), pesticide exposure can impair both the immune and detoxification system of honeybees, leading to increased susceptibility to parasites (Straub *et al.* 2019; Annoscia *et al.* 2020).

CONCLUSION

In the context of widespread insect and pollinator decline (Potts *et al.* 2016; McDermott 2021), honeybee health has long been a point of discussion in the apiculture and scientific community (Hassler *et al.* 2021). This critical eusocial pollinator encounters a variety of biotic and abiotic stressors during foraging and nesting. Further research is required to investigate other potential factors that may plausibly affect honeybee physiology, such as electromagnetic radiation (Molina-Montenegro *et al.* 2023). Generally, a combined effect of multiple stressors is likely to be more harmful than a single stressor (Goulson *et al.* 2015; Goulson & Nicholls 2022). It can be argued that the interaction among multiple stressors, varying spatially and temporally, is the key factor underlying the core issue of global honeybee health.

ACKNOWLEDGMENTS

The financial support was granted by the National Natural Science Foundation of China (32272935, Z.L.), the COLOSS Ricola Award for Excellence (Z.L.), the Earmarked Fund for Modern Agro-industry Technology Research System (CARS-44, T.J.), and the Lvyangjinfeng Program of Yangzhou (YZLYJFJH2021YXBS155, Z.L.).

CONFLICT OF INTEREST

The authors declare no competing financial interests.

REFERENCES

Acosta-Reyes F, Neupane R, Frank J, Fernández IS (2019). The Israeli acute paralysis virus IRES captures host ribosomes by mimicking a ribosomal state with hybrid tRNAs. *The EMBO Journal* **38**, e102226.

Aizen MA, Aguiar S, Biesmeijer JC *et al.* (2019). Global agricultural productivity is threatened by increasing pollinator dependence without a parallel increase in crop diversification. *Global Change Biology* **25**, 3516–27.

Al Naggar Y, Dabour K, Masry S, Sadek A, Naiem E, Giesy JP (2020). Sublethal effects of chronic exposure to CdO or PbO nanoparticles or their binary mixture on the honey bee (*Apis millefera* L.). *Environmental Science and Pollution Research* **27**, 19004–15.

Alonso-Salces RM, Cugnata NM, Guaspari E *et al.* (2017). Natural strategies for the control of *Paenibacillus larvae*, the causative agent of American foulbrood in honey bees: a review. *Apidologie* **48**, 387–400.

Amdam GV, Norberg K, Hagen A, Omholt SW (2003). Social exploitation of vitellogenin. *PNAS* **100**, 1799–802.

Anbumani S, Kakkar P (2018). Ecotoxicological effects of microplastics on biota: A review. *Environmental Science and Pollution Research* **25**, 14373–96.

Annoscia D, Di Prisco G, Becchimanzi A *et al.* (2020). Neonicotinoid clothianidin reduces honey bee immune response and contributes to *Varroa* mite proliferation. *Nature Communications* **11**, 5887.

Arrese EL, Soulages JL (2010). Insect fat body: Energy, metabolism, and regulation. *Annual Review of Entomology* **55**, 207–25.

Aufauvre J, Biron DG, Vidau C *et al.* (2012). Parasite-insecticide interactions: A case study of *Nosema ceranae* and fipronil synergy on honeybee. *Scientific Reports* **2**, 326.

Balzani P, Galeotti G, Scheggi S, Masoni A, Santini G, Baracchi D (2022). Acute and chronic ingestion of polyethylene (PE) microplastics has mild effects on honey bee health and cognition. *Environmental Pollution* **305**, 119318.

Barbet-Massin M, Rome Q, Muller F, Perrard A, Villemant C, Jiguet F (2013). Climate change increases the risk of invasion by the yellow-legged hornet. *Biological Conservation* **157**, 4–10.

Bargańska Ż, Ślebioda M, Namieśnik J (2016). Honey bees and their products: Bioindicators of environmental contamination. *Critical Reviews in Environmental Science and Technology* **46**, 235–48.

Beaurepaire A, Piot N, Doublet V *et al.* (2020). Diversity and global distribution of viruses of the western honey bee, *Apis mellifera*. *Insects* **11**, 239.

Ben Abdelkader F, Çakmak İ, Çakmak SS *et al.* (2021). Toxicity assessment of chronic exposure to common insecticides and bee medications on colony development and drones sperm parameters. *Ecotoxicology* **30**, 806–17.

Britton NF, Jane White KA (2021). The effect of covert and overt infections on disease dynamics in honey-bee colonies. *Bulletin of Mathematical Biology* **83**, 67.

Brown A, Rodriguez V, Pfister J, Perreten V, Neumann P, Retschnig G (2022). The dose makes the poison: feeding of antibiotic-treated winter honey bees. *Apis mellifera*, with probiotics and b-vitamins. *Apidologie* **53**, 19.

Buawangpong N, De Guzman LI, Khongphinitbunjong K, Frake AM, Burgett M, Chantawannakul P (2015). Prevalence and reproduction of *Tropilaelaps mercedesae* and *Varroa destructor* in concurrently infested *Apis mellifera* colonies. *Apidologie* **46**, 779–86.

Buteler M, Alma AM, Stadler T, Gingold AC, Manattini MC, Lozada M (2022). Acute toxicity of microplastic fibers to honeybees and effects on foraging behavior. *Science of the Total Environment* **822**, 153320.

Büchler R, Berg S, Le Conte Y (2010). Breeding for resistance to *Varroa destructor* in Europe. *Apidologie* **41**, 393–408.

Bąk B, Wilde J (2015). Grooming behavior by worker bees of various subspecies of honey bees to remove *Varroa destructor* mites. *Journal of Apicultural Research* **54**, 207–15.

Burden CM (2016). Sublethal effects of heavy metal and metalloid exposure in honey bees: behavioral modifications and potential mechanisms (Thesis). Arizona State University, Phoenix, Arizona.

Capitani G, Papa G, Pellecchia M, Negri I (2021). Disentangling multiple PM emission sources in the Po Valley (Italy) using honey bees. *Heliyon* **7**, e06194.

Castelli L, Branchiccela B, Garrido M *et al.* (2020). Impact of nutritional stress on honeybee gut microbiota, immunity, and *Nosema ceranae* Infection. *Microbial Ecology* **80**, 908–19.

Cebotari V, Buzu I, Postolachi O (2019). Impact of climate change of air temperature on vital activity of the bee families. *Scientific Papers Series D Animal Science* **62**, 249–55.

Chaimanee V, Evans JD, Chen Y, Jackson C, Pettis JS (2016). Sperm viability and gene expression in honey bee queens (*Apis mellifera*) following exposure to the neonicotinoid insecticide imidacloprid and the organophosphate acaricide coumaphos. *Journal of Insect Physiology* **89**, 1–8.

Chantawannakul P, Ramsey S, Vanengelsdorp D, Khongphinitbunjong K, Phokasem P (2018). *Tropilaelaps* mite: An emerging threat to European honey bee. *Current Opinion in Insect Science* **26**, 69–75.

Chen Y, Evans J, Feldlaufer M (2006a). Horizontal and vertical transmission of viruses in the honey bee, *Apis mellifera*. *Journal of Invertebrate Pathology* **92**, 152–9.

Chen Y, Evans JD, Smith IB, Pettis JS (2008). *Nosema ceranae* is a long-present and wide-spread microsporidian infection of the European honey bee (*Apis mellifera*) in the United States. *Journal of Invertebrate Pathology* **97**, 186–8.

Chen YP, Pettis JS, Collins A, Feldlaufer MF (2006b). Prevalence and transmission of honeybee viruses. *Applied and Environmental Microbiology* **72**, 606–11.

Cho Y, Jeong S, Lee D *et al.* (2021). Foraging trip duration of honeybee increases during a poor air quality episode and the increase persists thereafter. *Ecology and Evolution* **11**, 1492–500.

Cilia G, Bortolotti L, Albertazzi S, Ghini S, Nanetti A (2022). Honey bee (*Apis mellifera* L.) colonies as bioindicators of environmental SARS-CoV-2 occurrence. *Science of The Total Environment* **805**, 150327.

Cornelissen B, Neumann P, Schweiger O (2019). Global warming promotes biological invasion of a honey bee pest. *Global Change Biology* **25**, 3642–55.

Costa A, Veca M, Barberis M *et al.* (2019). Heavy metals on honeybees indicate their concentration in the atmosphere. A proof of concept. *Italian Journal of Animal Science* **18**, 309–15.

Costa CP, Leza M, Duennes MA *et al.* (2022). Pollen diet mediates how pesticide exposure impacts brain gene expression in nest-founding bumble bee queens. *Science of the Total Environment* **833**, 155216.

Cox KD, Covernton GA, Davies HL, Dower JF, Juanes F, Dudas SE (2019). Human consumption of microplastics. *Environmental Science & Technology* **53**, 7068–74.

Crowl TA, Crist TO, Parmenter RR, Belovsky G, Lugo AE (2008). The spread of invasive species and infectious disease as drivers of ecosystem change. *Frontiers in Ecology and the Environment* **6**, 238–46.

Cunningham MM, Tran L, Mckee CG *et al.* (2022). Honey bees as biomonitors of environmental contaminants, pathogens, and climate change. *Ecological Indicators* **134**, 108457.

Dargas JHF, Chaves SR, Fischer E (2016). Pollination of lark daisy on roadsides declines as traffic speed increases along an Amazonian highway. *Plant Biology* **18**, 542–4.

De Guzman LI, Williams GR, Khongphinitbunjong K, Chantawannakul P (2017). Ecology, life history, and management of *Tropilaelaps* mites. *Journal of Economic Entomology* **110**, 319–32.

De Jong D, Morse RA, Eickwort GC (1982). Mite pests of honey bees. *Annual Review of Entomology* **27**, 229–52.

De Jongh EJ, Harper SL, Yamamoto SS *et al.* (2022). One Health, One Hive: A scoping review of honey bees, climate change, pollutants, and antimicrobial resistance. *PLoS ONE* **17**, e0242393.

De León-Door AP, Pérez-Ordóñez G, Romo-Chacón A *et al.* (2020). Pathogenesis, epidemiology and variants of *Melissococcus plutonius*, the causal agent of European foulbrood. *Journal of Apicultural Science* **64**, 173–88.

Deng Y, Jiang X, Zhao H *et al.* (2021). Microplastic polystyrene ingestion promotes the susceptibility of honeybee to viral infection. *Environmental Science & Technology* **55**, 11680–92.

Deng Y, Yang S, Zhao H, Luo J, Yang W, Hou C (2022). Antibiotics-induced changes in intestinal bacteria result in the sensitivity of honey bee to virus. *Environmental Pollution* **314**, 120278.

Deroost K, Pham T-T, Opdenakker G, Van Den Steen PE (2015). The immunological balance between host and parasite in malaria. *FEMS Microbiology Reviews* **40**, 208–57.

Desneux N, Decourtye A, Delpuech J-M (2007). The sublethal effects of pesticides on beneficial arthropods. *Annual Review of Entomology* **52**, 81–106.

Devi S, Rana K, Negi N, Sharma HK, Thakur M (2021). Seasonal incidence of brood diseases in hives of Asian honey bee (*Apis cerana* F.) correlates with colony and weather parameters. *The Pharma Innovation Journal* **10**, 1945–51.

Di Prisco G, Annoscia D, Margiotta M *et al.* (2016). A mutualistic symbiosis between a parasitic mite and a pathogenic virus undermines honey bee immunity and health. *PNAS* **113**, 3203–8.

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. *PNAS* **110**, 18466–71.

Di Prisco G, Pennacchio F, Caprio E, Boncristiani HF Jr, Evans JD, Chen Y (2011). *Varroa destructor* is an effective vector of Israeli acute paralysis virus in the honeybee, *Apis mellifera*. *Journal of General Virology* **92**, 151–5.

Diaz-Basantes MF, Conesa JA, Fullana A (2020). Microplastics in honey, beer, milk and refreshments in Ecuador as emerging contaminants. *Sustainability* **12**, 5514.

Dickel F, Bos NMP, Hughes H *et al.* (2022). The oral vaccination with *Paenibacillus larvae* bacterin can decrease susceptibility to American Foulbrood infection in honey bees-A safety and efficacy study. *Frontiers in Veterinary Science* **9**, 946237.

Dietemann V, Pflugfelder J, Anderson D *et al.* (2012). *Varroa destructor*: Research avenues towards sustainable control. *Journal of Apicultural Research* **51**, 125–32.

Dolezal AG, Toth AL (2018). Feedbacks between nutrition and disease in honey bee health. *Current Opinion in Insect Science* **26**, 114–9.

DÈmares FJ, Crous KL, Pirk CWW, Nicolson SW, Human H (2016). Sucrose sensitivity of honey bees is differently affected by dietary protein and a neonicotinoid pesticide. *PLoS ONE* **11**, e0156584.

Edo C, Fernández-Alba AR, Vejsnæs F, Van Der Steen JJM, Fernández-Piñas F, Rosal R (2021). Honeybees as active samplers for microplastics. *Science of The Total Environment* **767**, 144481.

Eiri DM, Nieh JC (2012). A nicotinic acetylcholine receptor agonist affects honey bee sucrose responsiveness and decreases waggle dancing. *Journal of Experimental Biology* **215**, 2022–9.

Evans JD, Lopez DL (2004). Bacterial probiotics induce an immune response in the honey bee (Hymenoptera: Apidae). *Journal of Economic Entomology* **97**, 752–6.

Evans JD, Mckenna D, Scully E *et al.* (2018). Genome of the small hive beetle (*Aethina tumida*, Coleoptera: Nitidulidae), a worldwide parasite of social bee colonies, provides insights into detoxification and herbivory. *GigaScience* **7**, giy138.

Feldhaar H, Otti O (2020). Pollutants and their interaction with diseases of social hymenoptera. *Insects* **11**, 153.

Fijen TPM, Scheper JA, Boom TM, Janssen N, Raemakers I, Kleijn D (2018). Insect pollination is at least as important for marketable crop yield as plant quality in a seed crop. *Ecology Letters* **21**, 1704–13.

Fisher A, Rangel J (2018). Exposure to pesticides during development negatively affects honey bee (*Apis mellifera*) drone sperm viability. *PLoS ONE* **13**, e0208630.

Flores JM, Gil-Lebrero S, Gámiz V, Rodríguez MI, Ortiz MA, Quiles FJ (2019). Effect of the climate change on honey bee colonies in a temperate Mediterranean zone assessed through remote hive weight monitoring system in conjunction with exhaustive colonies assessment. *Science of The Total Environment* **653**, 1111–9.

Forrest JRK (2015). Plant–pollinator interactions and phenological change: What can we learn about climate impacts from experiments and observations? *Oikos* **124**, 4–13.

Gajda AM, Mazur ED, Bober AM, Czopowicz M (2021). *Nosema ceranae* interactions with *Nosema apis* and black queen cell virus. *Agriculture* **11**, 963.

Gao J, Ma S, Wang X *et al.* (2021). *Tropilaelaps mercedesae* parasitism changes behavior and gene expression in honey bee workers. *PLoS Pathogens* **17**, e1009684.

Garibaldi LA, Sáez A, Aizen MA, Fijen T, Bartomeus I (2020). Crop pollination management needs flower–visitor monitoring and target values. *Journal of Applied Ecology* **57**, 664–70.

Geslin B, Gauzens B, Baude M *et al.* (2017). Chapter Four—Massively introduced managed species and their consequences for plant–pollinator interactions. *Advances in Ecological Research* **57**, 147–99.

Ghazoul J (2005). Buzziness as usual? Questioning the global pollination crisis. *Trends in Ecology & Evolution* **20**, 367–73.

Gleadow R, Hanan J, Dorin A (2019). Averting robo-bees: Why free-flying robotic bees are a bad idea. *Emerging Topics in Life Sciences* **3**, 723–9.

Gong H, Chen X, Chen Y *et al.* (2016). Evidence of *Apis cerana* Sacbrood virus infection in *Apis mellifera*. *Applied and Environmental Microbiology* **82**, 2256–62.

Goretti E, Pallottini M, Rossi R *et al.* (2020). Heavy metal bioaccumulation in honey bee matrix, an indicator to assess the contamination level in terrestrial environments. *Environmental Pollution* **256**, 113388.

Goulson D, Nicholls E (2022). Anthropogenic influences on bee foraging. *Science* **375**, 970–2.

Goulson D, Nicholls E, Botías C, Rotheray EL (2015). Bee declines driven by combined stress from parasites, pesticides, and lack of flowers. *Science* **347**, 12559 57.

Grindrod I, Martin SJ (2021). Spatial distribution of recapping behaviour indicates clustering around *Varroa* infested cells. *Journal of Apicultural Research* **60**, 707–16.

Grozinger CM, Flenniken ML (2019). Bee viruses: Ecology, pathogenicity, and impacts. *Annual Review of Entomology* **64**, 205–26.

Guo Y, Goodman CL, Stanley DW, Bonning BC (2020). Cell lines for honey bee virus research. *Viruses* **12**, 236.

Gutiérrez M, Molero R, Gaju M, Van Der Steen J, Porrini C, Ruiz JA (2020). Assessing heavy metal pollution by biomonitoring honeybee nectar in Córdoba (Spain). *Environmental Science and Pollution Research* **27**, 10436–48.

Hassler EE, Cazier JA, Hopkins B, Wilkes JT, Smith K, Rünzel M (2021). A century of discovery: Mining 100 years of honey bee research. *Journal of Apicultural Research* **60**, 3–12.

Hegland SJ, Nielsen A, Lázaro A, Bjerknes A-L, Totland Ø (2009). How does climate warming affect plant-pollinator interactions? *Ecology Letters* **12**, 184–95.

Henry M, Beguin M, Requier F *et al.* (2012). A common pesticide decreases foraging success and survival in honey bees. *Science* **336**, 348–50.

Herrero-Latorre C, Barciela-García J, García-Martín S, Peña-Crecente RM (2017). The use of honeybees and honey as environmental bioindicators for metals and radionuclides: A review. *Environmental Reviews* **25**, 463–80.

Higes M, Martín-Hernández R, Botías C *et al.* (2008). How natural infection by *Nosema ceranae* causes honeybee colony collapse. *Environmental Microbiology* **10**, 2659–69.

Hopkins BK, Herr C, Sheppard WS (2012). Sequential generations of honey bee (*Apis mellifera*) queens produced using cryopreserved semen. *Reproduction, Fertility and Development* **24**, 1079–83.

Hristov P, Shumkova R, Palova N, Neov B (2020). Factors associated with honey bee colony losses: A mini-review. *Veterinary Sciences* **7**, 166.

Hulme PE (2014). Invasive species challenge the global response to emerging diseases. *Trends in Parasitology* **30**, 267–70.

Idrissou FO, Huang Q, Yañez O, Neumann P (2019). International beeswax trade facilitates small hive beetle invasions. *Scientific Reports* **9**, 10665.

Jaffé R, Veiga JC, Pope NS *et al.* (2019). Landscape genomics to the rescue of a tropical bee threatened by habitat loss and climate change. *Evolutionary Applications* **12**, 1164–77.

Jamal ZA, Abou-Shaara HF, Qamer S *et al.* (2021). Future expansion of small hive beetles, *Aethina tumida*, towards North Africa and South Europe based on temperature factors using maximum entropy algorithm. *Journal of King Saud University - Science* **33**, 101242.

Kairo G, Provost B, Tchamitchian S *et al.* (2016). Drone exposure to the systemic insecticide Fipronil indirectly impairs queen reproductive potential. *Scientific Reports* **6**, 319.

Kakumanu ML, Reeves AM, Anderson TD, Rodrigues RR, Williams MA (2016). Honey bee gut microbiome is altered by in-hive pesticide exposures. *Frontiers in Microbiology* **7**, 1255.

Kalynych S, Füzik T, Přidal A, De Miranda J, Plevka P (2017). Cryo-EM study of slow bee paralysis virus at low pH reveals iflavirus genome release mechanism. *PNAS* **114**, 598–603.

Keeler AM, Rose-Person A, Rafferty NE (2021). From the ground up: Building predictions for how climate change will affect belowground mutualisms, floral traits, and bee behavior. *Climate Change Ecology* **1**, 100013.

Khalifa SAM, Elshafiey EH, Shetaia AA *et al.* (2021). Overview of bee pollination and its economic value for crop production. *Insects* **12**, 688.

Kraus B, Page RE Jr (1995). Effect of *Varroa jacobsoni* (Mesostigmata: Varroidae) on feral *Apis mellifera* (Hymenoptera: Apidae) in California. *Environmental Entomology* **24**, 1473–80.

Kwong WK, Moran NA (2016). Gut microbial communities of social bees. *Nature Reviews Microbiology* **14**, 374–84.

Le Conte Y, Meixner MD, Brandt A *et al.* (2020). Geographical distribution and selection of european honey bees resistant to *Varroa destructor*. *Insects* **11**, 873.

Leclercq G, Pannebakker B, Gengler N, Nguyen BK, Francis F (2017). Drawbacks and benefits of hygienic behavior in honey bees (*Apis mellifera* L.): A review. *Journal of Apicultural Research* **56**, 366–75.

Leong M, Ponisio LC, Kremen C, Thorp RW, Roderick GK (2016). Temporal dynamics influenced by global change: Bee community phenology in urban, agricultural, and natural landscapes. *Global Change Biology* **22**, 1046–53.

Lin Z, Page P, Li L *et al.* (2016). Go east for better honey bee health: *Apis cerana* is faster at hygienic behavior than *A. mellifera*. *PLoS ONE* **11**, e0162647.

Lin Z, Qin Y, Page P *et al.* (2018). Reproduction of parasitic mites *Varroa destructor* in original and new honeybee hosts. *Ecology and Evolution* **8**, 2135–45.

Lin Z, Wang S, Neumann P *et al.* (2021a). Population genetics and host specificity of *Varroa destructor* mites infesting eastern and western honeybees. *Journal of Pest Science* **94**, 1487–504.

Lin Z, Zhang N, Wang Z *et al.* (2022). Acute and chronic viruses mediated by an ectoparasite targeting different developmental stages of honeybee (*Apis mellifera* and *Apis cerana*) brood. *Frontiers in Veterinary Science* **9**, 951159.

Lin Z, Zhao L, Cao L *et al.* (2021b). A survey of common pathogens of *Apis* spp. In wild non-cave honeybees in Southwest China. *Journal of Wildlife Diseases* **57**, 932–5.

Lindgren E, Andersson Y, Suk JE, Sudre B, Semenza JC (2012). Monitoring EU emerging infectious disease risk due to climate change. *Science* **336**, 418–9.

Locke B (2016). Natural *Varroa* mite-surviving *Apis mellifera* honeybee populations. *Apidologie* **47**, 467–82.

Lin Z, Zhu Z, Zhuang M *et al.* (2023). Effects of local domestication warrant attention in honey bee population genetics. *Science Advances* **9**, eade7917.

Mallinger RE, Gaines-Day HR, Gratton C (2017). Do managed bees have negative effects on wild bees?: A systematic review of the literature. *PLoS ONE* **12**, e0189268.

Mammo FK, Amoah ID, Gani KM *et al.* (2020). Microplastics in the environment: Interactions with microbes and chemical contaminants. *Science of The Total Environment* **743**, 140518.

Mao W, Schuler MA, Berenbaum MR (2013). Honey constituents up-regulate detoxification and immunity genes in the western honey bee *Apis mellifera*. *PNAS* **110**, 8842–6.

Marshman J, Blay-Palmer A, Landman K (2019). Anthropocene crisis: Climate change, pollinators, and food security. *Environments* **6**, 22.

Martin SJ, Highfield AC, Brettell L *et al.* (2012). Global honey bee viral landscape altered by a parasitic mite. *Science* **336**, 1304–6.

Martín-Hernández R, Bartolomé C, Chejanovsky N *et al.* (2018). *Nosema ceranae* in *Apis mellifera*: A 12 years postdetection perspective. *Environmental Microbiology* **20**, 1302–29.

Mcafee A, Chapman A, Higo H *et al.* (2020). Vulnerability of honey bee queens to heat-induced loss of fertility. *Nature Sustainability* **3**, 367–76.

Mccabe LM, Aslan CE, Cobb NS (2022). Decreased bee emergence along an elevation gradient: Implications for climate change revealed by a transplant experiment. *Ecology* **103**, e03598.

Mcdermott A (2021). To understand the plight of insects, entomologists look to the past. *PNAS* **118**, e2018499117.

Mcmenamin AJ, Flenniken ML (2018). Recently identified bee viruses and their impact on bee pollinators. *Current Opinion in Insect Science* **26**, 120–9.

Medrzycki P, Sgolastra F, Bortolotti L *et al.* (2010). Influence of brood rearing temperature on honey bee development and susceptibility to poisoning by pesticides. *Journal of Apicultural Research* **49**, 52–9.

Millard J, Outhwaite CL, Kinnersley R *et al.* (2021). Global effects of land-use intensity on local pollinator biodiversity. *Nature Communications* **12**, 2902.

Molina-Montenegro MA, Acuña-Rodríguez IS, Ballesteros GI *et al.* (2023). Electromagnetic fields disrupt the pollination service by honeybees. *Science Advances* **9**, eadh1455.

Mondet F, Alaux C, Severac D, Rohmer M, Mercer AR, Le Conte Y (2015). Antennae hold a key to *Varroa*-sensitive hygiene behaviour in honey bees. *Scientific Reports* **5**, 10454.

Morales MM, Ramos MJG, Vázquez PP *et al.* (2020). Distribution of chemical residues in the beehive compartments and their transfer to the honeybee brood. *Science of The Total Environment* **710**, 136288.

Moritz RFA, Härtel S, Neumann P (2005). Global invasions of the western honeybee (*Apis mellifera*) and the consequences for biodiversity. *Ecoscience* **12**, 289–301.

Motta EV, Raymann K, Moran NA (2018). Glyphosate perturbs the gut microbiota of honey bees. *PNAS* **115**, 10305–10.

Muth F, Francis JS, Leonard AS (2019). Modality-specific impairment of learning by a neonicotinoid pesticide. *Biology Letters* **15**, 20190359.

Muth F, Leonard A (2019). A neonicotinoid pesticide impairs foraging, but not learning, in free-flying bumblebees. *Scientific Reports* **9**, 4764.

Nazzi F, Le Conte Y (2016). Ecology of *Varroa destructor*, the major ectoparasite of the western honey bee, *Apis mellifera*. *Annual Review of Entomology* **61**, 417–32.

Neumann P, Blacquière T (2017). The Darwin cure for apiculture? Natural selection and managed honeybee health. *Evolutionary Applications* **10**, 226–30.

Neumann P, Carreck N (2010). Honey bee colony losses. *Journal of Apicultural Research* **49**, 1–6.

Neumann P, Pettis JS, Schäfer MO (2016). Quo vadis *Aethina tumida*? Biology and control of small hive beetles. *Apidologie* **47**, 427–66.

Nganso BT, Fombong AT, Yusuf AA, Pirk CWW, Stuhl C, Torto B (2017). Hygienic and grooming behaviors in African and European honeybees—New damage categories in *Varroa destructor*. *PLoS ONE* **12**, e0179329.

Nganso BT, Fombong AT, Yusuf AA, Pirk CWW, Stuhl C, Torto B (2018). Low fertility, fecundity and numbers of mated female offspring explain the lower reproductive success of the parasitic mite *Varroa destructor* in African honeybees. *Parasitology* **145**, 1633–9.

O'neal ST, Anderson TD, Wu-Smart JY (2018). Interactions between pesticides and pathogen susceptibility in honey bees. *Current Opinion in Insect Science* **26**, 57–62.

Oddie MA, Dahle B, Neumann P (2017). Norwegian honey bees surviving *Varroa destructor* mite infestations by means of natural selection. *PeerJ* **5**, e3956.

Oddie MAY, Burke A, Dahle B, Le Conte Y, Mondet F, Locke B (2021). Reproductive success of the parasitic mite (*Varroa destructor*) is lower in honeybee colonies that target infested cells with recapping. *Scientific Reports* **11**, 9133.

Odemer R, Alkassab AT, Bischoff G *et al.* (2020). Chronic high glyphosate exposure delays individual worker bee (*Apis mellifera* L.) development under field conditions. *Insects* **11**, 664.

Oldroyd BP (2007). What's killing American honey bees? *PLoS Biology* **5**, e168.

Page P, Lin Z, Buawangpong N *et al.* (2016). Social apoptosis in honey bee superorganisms. *Scientific Reports* **6**, 27210.

Papa G, Capitani G, Capri E, Pellecchia M, Negri I (2021). Vehicle-derived ultrafine particulate contaminating bees and bee products. *Science of The Total Environment* **750**, 141700.

Paray BA, Kumari I, Hajam YA *et al.* (2021). Honeybee nutrition and pollen substitutes: A review. *Saudi Journal of Biological Sciences* **28**, 1167–76.

Paris L, El Alaoui H, Delbac F, Diogon M (2018). Effects of the gut parasite *Nosema ceranae* on honey bee physiology and behavior. *Current Opinion in Insect Science* **26**, 149–54.

Paris L, Peghaire E, Moné A *et al.* (2020). Honeybee gut microbiota dysbiosis in pesticide/parasite co-exposures is mainly induced by *Nosema ceranae*. *Journal of Invertebrate Pathology* **172**, 107348.

Phillips BB, Bullock JM, Gaston KJ *et al.* (2021). Impacts of multiple pollutants on pollinator activity in road verges. *Journal of Applied Ecology* **58**, 1017–29.

Phillips BB, Wallace C, Roberts BR *et al.* (2020). Enhancing road verges to aid pollinator conservation: A review. *Biological Conservation* **250**, 108687.

Piot N, Schweiger O, Meeus I *et al.* (2022). Honey bees and climate explain viral prevalence in wild bee communities on a continental scale. *Scientific Reports* **12**, 1904.

Pirk CWW, Crewe RM, Moritz RFA (2017). Risks and benefits of the biological interface between managed and wild bee pollinators. *Functional Ecology* **31**, 47–55.

Pirk CWW, Strauss U, Yusuf A, Démares F, Human H (2016). Honeybee health in Africa—A review. *Apidologie* **47**, 276–300.

Porto RG, De Almeida RF, Cruz-Neto O *et al.* (2020). Pollination ecosystem services: A comprehensive review of economic values, research funding and policy actions. *Food Security* **12**, 1425–42.

Posada-Florez F, Sonenshine DE, Egekwu NI, Rice C, Lupitskyy R, Cook SC (2019). Insights into the metabolism and behaviour of *Varroa destructor* mites from analysis of their waste excretions. *Parasitology* **146**, 527–32.

Potts SG, Imperatriz-Fonseca V, Ngo HT *et al.* (2016). Safeguarding pollinators and their values to human well-being. *Nature* **540**, 220–9.

Potts SG, Neumann P, Vaissière B, Vereecken NJ (2018). Robotic bees for crop pollination: Why drones cannot replace biodiversity. *Science of The Total Environment* **642**, 665–7.

Preston DL, Mischler JA, Townsend AR, Johnson PTJ (2016). Disease ecology meets ecosystem science. *Ecosystems* **19**, 737–48.

Procházková M, FüZik T, Škubník K *et al.* (2018). Virion structure and genome delivery mechanism of sacbrood honeybee virus. *PNAS* **115**, 7759–64.

Procházková M, Škubník K, Füzik T, Mukhamedova L, Přidal A, Plevka P (2020). Virion structures and genome delivery of honeybee viruses. *Current Opinion in Virology* **45**, 17–24.

Pusceddu M, Cini A, Alberti S *et al.* (2021). Honey bees increase social distancing when facing the ectoparasite *Varroa destructor*. *Science Advances* **7**, eabj1398.

Quigley TP, Amdam GV, Harwood GH (2019). Honey bees as bioindicators of changing global agricultural landscapes. *Current Opinion in Insect Science* **35**, 132–7.

Ramsey S, Gulbronson CJ, Mowery J, Ochoa R, Vanengelsdorp D, Bauchan G (2018). A multimicroscopy approach to discover the feeding site and host tissue consumed by *Varroa destructor* on host honey bees. *Microscopy and Microanalysis* **24**, 1258–9.

Ramsey SD, Ochoa R, Bauchan G *et al.* (2019). *Varroa destructor* feeds primarily on honey bee fat body tissue and not hemolymph. *PNAS* **116**, 1792–801.

Rangel J, Tarpy DR (2015). The combined effects of miticides on the mating health of honey bee (*Apis mellifera* L.) queens. *Journal of Apicultural Research* **54**, 275–83.

Raven PH, Wagner DL (2021). Agricultural intensification and climate change are rapidly decreasing insect biodiversity. *PNAS* **118**, e2002548117.

Raymann K, Motta EV, Girard C, Riddington IM, Dinser JA, Moran NA (2018). Imidacloprid decreases honey bee survival rates but does not affect the gut microbiome. *Applied and Environmental Microbiology* **84**, e00545–18.

Requier F, Rome Q, Chiron G *et al.* (2019). Predation of the invasive Asian hornet affects foraging activity and survival probability of honey bees in Western Europe. *Journal of Pest Science* **92**, 567–78.

Rigaud T, Perrot-Minnot M-J, Brown MJF (2010). Parasite and host assemblages: Embracing the reality will improve our knowledge of parasite transmission and virulence. *Proceedings of the Royal Society B: Biological Sciences* **277**, 3693–702.

Ryabov EV, Posada-Florez F, Rogers C *et al.* (2022). The vectoring competence of the mite *Varroa destructor* for deformed wing virus of honey bees is dynamic and affects survival of the mite. *Frontiers in Insect Science* **2**, 931352.

Sales K, Vasudeva R, Dickinson ME *et al.* (2018). Experimental heatwaves compromise sperm function and cause transgenerational damage in a model insect. *Nature Communications* **9**, 4771.

Sayğı H (2020). Adverse effects of climate change on agriculture: An evaluation of fruit and honey bee farming. *Asian Journal of Agriculture and Rural Development* **10**, 504–14.

Seeley TD, Smith ML (2015). Crowding honeybee colonies in apiaries can increase their vulnerability to the deadly ectoparasite *Varroa destructor*. *Apidologie* **46**, 716–27.

Seibold S, Gossner MM, Simons NK *et al.* (2019). Arthropod decline in grasslands and forests is associated with landscape-level drivers. *Nature* **574**, 671–4.

Simeunovic P, Stevanovic J, Cirkovic D *et al.* (2014). *Nosema ceranae* and queen age influence the reproduction and productivity of the honey bee colony. *Journal of Apicultural Research* **53**, 545–54.

Siviter H, Bailes EJ, Martin CD *et al.* (2021). Agrochemicals interact synergistically to increase bee mortality. *Nature* **596**, 389–92.

Smith KE, Weis D (2022). Metal and Pb isotope characterization of particulates encountered by foraging honeybees in Metro Vancouver. *Science of the Total Environment* **826**, 154181.

Spurny R, Přidal A, Pálková L, Kiem HKT, De Miranda JR, Plevka P (2017). Virion structure of black queen cell virus, a common honeybee pathogen. *Journal of Virology* **91**, e02100–16.

Stanisavljević L, Partap U, IPBES (2016). Assessment report on pollinators, pollination and food production. IPBES, Bonn, Germany. https://digitallibrary.un.org/record/3794027.

Steinhauer N, Kulhanek K, Antúnez K *et al.* (2018). Drivers of colony losses. *Current Opinion in Insect Science* **26**, 142–8.

Straub L, Villamar-Bouza L, Bruckner S, Chantawannakul P, Gauthier L, Khongphinitbunjong K (2016). Neonicotinoid insecticides can serve as inadvertent insect contraceptives. *Proceedings of the Royal Society B: Biological Sciences* **283**, 20160506.

Straub L, Villamar-Bouza L, Bruckner S, Chantawannakul P, Kolari E, Maitip J (2021). Negative effects of neonicotinoids on male honeybee survival, behaviour and physiology in the field. *Journal of Applied Ecology* **58**, 2515–28.

Straub L, Williams GR, Vidondo B, Khongphinitbunjong K, Retschnig G, Schneeberger A (2019). Neonicotinoids and ectoparasitic mites synergistically impact honeybees. *Scientific Reports* **9**, 8159.

Strauss U, Dietemann V, Human H, Crewe RM, Pirk CWW (2016). Resistance rather than tolerance explains survival of savannah honeybees (*Apis mellifera scutellata*) to infestation by the parasitic mite *Varroa destructor*. *Parasitology* **143**, 374–87.

Sánchez-Bayo F, Goulson D, Pennacchio F, Nazzi F, Goka K, Desneux N (2016). Are bee diseases linked to pesticides?—A brief review. *Environment international* **89**, 7–11.

Škubník K, Nováček J, Füzik T, Přidal A, Paxton RJ, Plevka P (2017). Structure of deformed wing virus, a major honey bee pathogen. *PNAS* **114**, 3210–5.

Škubník K, Sukeník L, Buchta D *et al.* (2021). Capsid opening enables genome release of iflaviruses. *Science Advances* **7**, eabd7130.

Tabor JA, Koch JB (2021). Ensemble models predict invasive bee habitat suitability will expand under future climate scenarios in Hawai'i. *Insects* **12**, 443.

Tan K, Radloff SE, Li JJ *et al.* (2007). Bee-hawking by the wasp, *Vespa velutina*, on the honeybees *Apis cerana* and *A. mellifera*. *Naturwissenschaften* **94**, 469–72.

Tan K, Wang C, Dong S, Li X, Nieh JC (2017). The pesticide flupyradifurone impairs olfactory learning in Asian honey bees (*Apis cerana*) exposed as larvae or as adults. *Scientific Reports* **7**, 17772.

Teeters BS, Johnson RM, Ellis MD, Siegfried BD (2012). Using video-tracking to assess sublethal effects of pesticides on honey bees (*Apis mellifera* L.). *Environmental Toxicology and Chemistry* **31**, 1349–54.

Theisen-Jones H, Bienefeld K (2016). The Asian honey bee (*Apis cerana*) is significantly in decline. *Bee World* **93**, 90–7.

Thimmegowda GG, Mullen S, Sottilare K *et al.* (2020). A field-based quantitative analysis of sublethal effects of air pollution on pollinators. *PNAS* **117**, 20653–61.

Tihelka E (2018). Effects of synthetic and organic acaricides on honey bee health: A review. *Slovenian Veterinary Research* **55**, 114–40.

Tong L, Nieh JC, Tosi S (2019). Combined nutritional stress and a new systemic pesticide (flupyradifurone, Sivanto®) reduce bee survival, food consumption, flight success, and thermoregulation. *Chemosphere* **237**, 124408.

Traynor KS, Mondet F, De Miranda JR *et al.* (2020). *Varroa destructor*: A complex parasite, crippling honey bees worldwide. *Trends in Parasitology* **36**, 592–606.

Tritschler M, Vollmann JJ, Yañez O, Chejanovsky N, Crailsheim K, Neumann P (2017). Protein nutrition governs within-host race of honey bee pathogens. *Scientific Reports* **7**, 14988.

Tsuruda JM, Chakrabarti P, Sagili RR (2021). Honey bee nutrition. *Veterinary Clinics: Food Animal Practice* **37**, 505–19.

Ullah A, Tlak Gajger I, Majoros A *et al.* (2021). Viral impacts on honey bee populations: A review. *Saudi Journal of Biological Sciences* **28**, 523–30.

Ulrich J, Bucher SF, Eisenhauer N *et al.* (2020). Invertebrate decline leads to shifts in plant species abundance and phenology. *Frontiers in Plant Science* **11**, 542125.

Van Der Sluijs JP (2020). Insect decline, an emerging global environmental risk. *Current Opinion in Environmental Sustainability* **46**, 39–42.

Vanbergen AJ, Espíndola A, Aizen MA (2018). Risks to pollinators and pollination from invasive alien species. *Nature Ecology & Evolution* **2**, 16.

Varela M, Spencer TE, Palmarini M, Arnaud F (2009). Friendly viruses: the special relationship between endogenous retroviruses and their host. *Annals of the New York Academy of Sciences* **1178**, 157–72.

Vaudo AD, Tooker JF, Grozinger CM, Patch HM (2015). Bee nutrition and floral resource restoration. *Current Opinion in Insect Science* **10**, 133–41.

Vercelli M, Novelli S, Ferrazzi P, Lentini G, Ferracini C (2021). A qualitative analysis of beekeepers' perceptions and farm management adaptations to the impact of climate change on honey bees. *Insects* **12**, 228.

Villa JD, Danka RG, Harris JW (2009). Simplified methods of evaluating colonies for levels of *Varroa* Sensitive Hygiene (VSH). *Journal of Apicultural Research* **48**, 162–7.

Walsh BS, Parratt SR, Hoffmann AA *et al.* (2019). The impact of climate change on fertility. *Trends in Ecology & Evolution* **34**, 249–59.

Walsh EM, Sweet S, Knap A, Rangel J (2020). Queen honey bee (*Apis mellifera*) pheromone and reproductive behavior are affected by pesticide exposure during development. *Behavioral Ecology and Sociobiology* **74**, 33.

Wang K, Cai M, Sun J *et al.* (2023). Atrazine exposure can dysregulate the immune system and increase the susceptibility against pathogens in honeybees in a dose-dependent manner. *Journal of Hazardous Materials* **452**, 131179.

Wang K, Chen H, Fan RL *et al.* (2022). Effect of carbendazim on honey bee health: Assessment of survival, pollen consumption, and gut microbiome composition. *Ecotoxicology and Environmental Safety* **239**, 113648.

Wang K, Chen H, Lin ZG *et al.* (2021a). Carbendazim exposure during the larval stage suppresses major royal jelly protein expression in nurse bees (*Apis mellifera*). *Chemosphere* **266**, 129011.

Wang K, Li J, Zhao L *et al.* (2021b). Gut microbiota protects honey bees (*Apis mellifera* L.) against polystyrene microplastics exposure risks. *Journal of Hazardous Materials* **402**, 123828.

Wang S, Chen G, Lin Z, Wu Y, Hu F, Zheng H (2019). Occurrence of multiple honeybee viruses in the ectoparasitic mites *Varroa* spp. in *Apis cerana* colonies. *Journal of Invertebrate Pathology* **166**, 107225.

Wang S, Lin Z, Chen G *et al.* (2020). Reproduction of ectoparasitic mites in a coevolved system: *Varroa* spp.-Eastern honey bees, *Apis cerana*. *Ecology and Evolution* **10**, 14359–71.

Wei R, Cao L, Feng Y, Chen Y, Chen G, Zheng H (2022). Sacbrood virus: A growing threat to honeybees and wild pollinators. *Viruses* **14**, 1871.

Werenkraut V, Arbetman MP, Fergnani PN (2022). The Oriental hornet (*Vespa orientalis* L.): A threat to the Americas? *Neotropical Entomology* **51**, 330–8.

Wheeler MM, Robinson GE (2014). Diet-dependent gene expression in honey bees: Honey vs. sucrose or high fructose corn syrup. *Scientific Reports* **4**, 5726.

Wickramasinghe K, Mathers JC, Wopereis S, Marsman DS, Griffiths JC (2020). From lifespan to healthspan: The role of nutrition in healthy ageing. *Journal of Nutritional Science* **9**, e33.

Williams GR, Troxler A, Retschnig G *et al.* (2015). Neonicotinoid pesticides severely affect honey bee queens. *Scientific Reports* **5**, 14621.

Wilson CJ, Jamieson MA (2019). The effects of urbanization on bee communities depends on floral resource availability and bee functional traits. *PLoS ONE* **14**, e0225852.

Woolhouse ME, Taylor LH, Haydon DT (2001). Population biology of multihost pathogens. *Science* **292**, 1109–12.

Wu JY, Anelli CM, Sheppard WS (2011). Sub-lethal effects of pesticide residues in brood comb on worker honey bee (*Apis mellifera*) development and longevity. *PLoS ONE* **6**, e14720.

Young HS, Parker IM, Gilbert GS, Sofia Guerra A, Nunn CL (2017). Introduced species, disease ecology, and biodiversity–disease relationships. *Trends in Ecology & Evolution* **32**, 41–54.

Zhang Y, Kang S, Allen S, Allen D, Gao T, Sillanpää M (2020). Atmospheric microplastics: A review on current status and perspectives. *Earth-Science Reviews* **203**, 103118.

Zheng H, Lin Z, Huang S, Sohr A, Wu L, Chen YP (2014). Spore loads may not be used alone as a direct indicator of the severity of *Nosema ceranae* Infection in honey bees *Apis mellifera* (Hymenoptera:Apidae). *Journal of Economic Entomology* **107**, 2037–44.

Zhu G, Gutierrez Illan J, Looney C, Crowder DW (2020). Assessing the ecological niche and invasion potential of the Asian giant hornet. *PNAS* **117**, 24646–8.

Cite this article as:

Lin Z, Shen S, Wang K, Ji T (2024). Biotic and abiotic stresses on honeybee health. *Integrative Zoology* **19,** 442–57. https://doi.org/10.1111/1749-4877.12752