The role of disease in bee foraging ecology

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Highlights

- Diseases have a central, but poorly understood role in bee foraging ecology

- Flowers are hubs for horizontal transmission of parasites within and between bee species

- Nutritional and non-nutritional pollen and nectar chemistry affects bee immunity and disease

- Diseases modify foraging behaviour by impairing foraging ability or changing floral preferences

- Parasites affect pollination services by reducing bee populations or changing foraging behaviour

Abstract

Diseases have important but understudied effects on bee foraging ecology. Bees transmit and contract diseases on flowers, but floral traits including plant volatiles and inflorescence architecture may affect transmission. Diseases spill over from managed or invasive pollinators to native wild bee species, and impacts of emerging diseases are of particular concern, threatening pollinator populations and pollination services. Here we review how parasites can alter the foraging behaviour of bees by changing floral preferences and impairing foraging efficiency. We also consider how changes to pollinator behaviours alter or reduce pollination services. The availability of diverse floral resources can, however, ameliorate bee diseases and their impacts through better nutrition and antimicrobial effects of plant compounds in pollen and nectar.

Introduction

Bees, and the pollination services they provide, are threatened by a range of factors, including habitat loss, climate change, pesticides, and parasites [1],[2]. The impacts of parasites, and the diseases they cause, may be enhanced by interactions with other stressors [3]. Pesticides and decreasing floral resources can make bees more susceptible and less tolerant to diseases [4],[5], and global trade of managed pollinators has led to the spread of diseases into novel areas and hosts [2],[6]. Parasites can be transmitted and contracted by foraging bees on flowers [7], whereas the floral food rewards - pollen and nectar - that are consumed by bees may modulate disease severity, for example, through the antimicrobial compounds they contain [8],[9]. Foraging behaviour can also be impaired or altered by diseases (e.g. [10]), potentially affecting pollination services. Bee diseases and foraging ecology are thus intricately linked in a number of ways, and a better understanding of these relationships will be crucial to control the spread and negative effects of bee diseases. This review outlines the interactions between disease and foraging in bees, and highlights recent advances in this field as well as critical knowledge gaps.

Foraging bees contract and transmit diseases on flowers

Flowers act as hubs for the spread of diseases among visiting pollinators [7],[11],[12],[13]. Diseased bees can deposit parasites on flowers, for example, through defecation during foraging, or simple contact between contaminated bee and flower surfaces. Parasites may also be vectored by uninfected bees between flowers [13]. Subsequent flower visiting bees may then contract infections [7],[14].Thus interactions at flowers present an important horizontal transmission route for bee diseases.

Emerging diseases spilling over from managed and naturalized honey bee and bumble bee colonies into native wild bee populations through shared flower use present a particular concern for pollinator conservation [15],[12],[16],[17]. For example, Deformed Wing Virus (DWV) and *Nosema ceranae* (Microsporidia) are both transmitted between honey bees and wild bumble bees, and can have high virulence in bumble bee hosts [12]. The detection of several viruses first described from honey bees in solitary bees, wasps, hoverflies, and moths suggests that some parasites may even be transmitted across broader taxonomic boundaries in the pollinator community [16],[18],[19]. However, it remains to be demonstrated if active and virulent viral infections can occur in these alternative hosts, as most studies to date have only screened for the presence, but not active replication of viruses, and effects on these alternative hosts remain unknown [19]. Global trade of honey bees has introduced bee parasites such as DWV strains into new areas where they were previously absent [6], which may threaten native pollinators. In South America, the invasive European bumble bee *Bombus terrestris* (introduced for greenhouse pollination in the 1990s) is likely to have spread the trypanosomatid gut parasite *Crithidia bombi* to native bumble bees, which may have contributed to the rapid decline of these keystone species [20]. However, the epidemiological processes of disease spread among native and invasive pollinators, as well as disease impacts on wild pollinator populations are not well understood, and further research in this area is needed urgently [19]. Next generation sequencing methods have greatly facilitated the detection of novel pathogens and other microbial associates of bees [21],[22], and can in the future be employed to characterize plant-pollinator-pathogen webs via metabarcoding or metagenomics [23].

Floral traits such as floral morphology or chemistry could influence pollinator disease transmission, with flowering plants varying in their likelihood of spreading infections [7],[11]. For example, floral volatiles that provide broad spectrum antimicrobial protection for the flower can inhibit the survival on or colonisation of flowers by microorganisms [24], and so could equally kill bee parasites. Furthermore, architectural complexity in inflorescences was found to reduce *C. bombi* transmission in *B. terrestris* [7]. To date, there is little knowledge on the specific interactions of floral traits and bee disease transmission [11]. However, anthropogenic changes to plant communities, like introduction of invasive plants or loss of floral diversity via intensified land use, could alter transmission patterns with unknown consequences for bee health [11].

The chemistry of bee forage impacts pollinator disease

The chemistry of pollen and nectar varies in both primary metabolites (e.g., sugars, amino acids, and lipids) and the secondary compounds like flavonoids, terpenoids, and alkaloids [25]. These nutritional and non-nutritional chemical differences could modulate parasite susceptibility and disease severity of bees. For example, nutrition has been linked to bee immunocompetence. Bumble bees fed on a protein deprived diet containing no pollen showed a reduced immune response to *C. bombi* infections [26]. In honey bee workers, protein-rich pollen types resulted in higher individual (phenoloxidase activity) and social (glucose oxidase activity) immunocompetence [4]. Furthermore, honey bee larvae were more susceptible to *Aspergillus* opportunistic fungal pathogens when fed on poorer larval diets with monofloral pollen in comparison to polyfloral pollen [27].

Conversely, a diet with a high nutritional value can also benefit the parasite. Logan et al. [28] reported higher *C. bombi* levels in bumble bees and Jack et al. [29] reported higher *N. ceranae* spore loads in honey bees when both hosts were fed on pollen. In this case, the survival of honey bees fed on pollen was enhanced despite increased *N. ceranae* parasite load compared with pollen starved bees. This suggests that although a rich diet may improve conditions for parasites, it also increases the host’s disease tolerance, which may be more important than parasite numbers alone [29].

The above studies did not directly manipulate individual chemical constituents of the experimental diets, making it difficult to determine what specific qualities of dietary variation influenced the different experimental outcomes. Pollen is chemically complex and highly variable between species, and the role of some pollen constituents like fatty acids, sterols, flavonoids, and alkaloids were neither investigated nor discussed. This important limitation will need to be addressed in future studies.

Plant secondary metabolites have a range of ecological functions, including defence against microbial disease. Although the chemistry of pollen and nectar is of increasing interest [25], knowledge of the diversity of these secondary compounds and their antimicrobial properties against bee diseases is limited. The best evidence to date that nectar secondary compounds reduce disease load in bees comes from several studies of *C. bombi* in bumble bees. Manson et al. [30] showed that gelsemine (an alkaloid found in the nectar of *Gelsemium sempervirens*) reduced *C. bombi* infection levels in *B. impatiens*. Richardson et al. [8] later found four out of eight secondary nectar compounds to inhibit *C. bombi* in the same host. Baracchi et al. [31] showed that nicotine delayed the development of *C. bombi* infections in a second host species, *B. terrestris*. Such effects can occur under biologically-realistic dosage levels, for example, in Richardson et al. [8] the monoterpene thymol was fed at 0.2 ppm in sugar water, whereas it naturally occurs in thyme nectar at concentrations of up to 8.2 ppm, sufficient to inhibit *C. bombi* in vitro [9]. The eco-evolutionary interactions between plant compounds and bee parasites are however likely considerably more complex than this, and have only been studied in a few cases. Palmer-Young et al. [9] showed that *C. bombi* strains differed more than 4-fold in their EC_{50} values for thymol and anabasine. *C. bombi* strains could also readily evolve increased resistance to thymol in vitro within a 6 week period [32]. Importantly, under natural conditions, parasites will not be exposed to single plant compounds within the host, but chemical mixtures from the bee diet. Different plant metabolites may then act additively or synergistically in inhibiting parasites, although this has been shown only using compounds at above naturally occurring concentrations [33].

In addition to direct effects, secondary plant compounds can indirectly affect bee diseases by modulating the immune system or gut microbiome. Mao et al. [34] showed that *p*-coumaric acid, a phenylpropanoid found in nectar and pollen, enabled upregulation of two antimicrobial peptides (abaecin and defensin) in honey bees, and Negri et al. [35] found an improved cellular immune response in honey bees feeding on abscisic acid, a terpenoid present in nectar of some species. A potential, but unstudied, path for secondary metabolites to indirectly affect bee parasites is through modulation of the bee gut microbiome, the composition of which has been shown to play an important role in parasite susceptibility [22],[36]. Given the complex interactions between plant compounds, microorganisms, and hosts, to understand the outcome for bee health it will be necessary to complement controlled laboratory experiments elucidating underlying mechanisms with field or semi-field (e.g. greenhouse) trials under more natural conditions. These studies should investigate fitness consequences of phytochemical dietary differences for healthy or diseased bees by manipulating the plant composition of the foraging environment or supplementing free flying bee colonies with target phytochemicals. Studies will also have to be extended beyond the bumble bee – *C. bombi* system, as patterns found in this interaction may not translate to other pathogens (e.g. viruses, *Nosema*) and hosts.

Besides naturally occurring plant compounds, bees are also exposed to agricultural pesticides during foraging. Neonicotinoid insecticides can suppress the immune system of honey bees [37], and increase the risk and severity of parasitic infections with *N. ceranae* and DWV [5],[38]. The interaction of pesticides and other anthropogenic stressors with diseases increases the pressure on pollinator populations [2],[3].

Ultimately, a biodiverse floral landscape and the resulting dietary alternatives for bees may have an important beneficial effect for bee disease resistance and tolerance by improving nutrition and availability of beneficial secondary compounds. Polyfloral diets increase immune function and decrease disease loads in honey bees [4],[39], and the different secondary compounds in nectar may act synergistically against parasites (e.g., *C. bombi* in bumble bees [33],[40]). One of the best and most practical methods to improve pollinator health may therefore be to ensure the availability of diverse and health promoting floral resources in urban, agricultural, and natural landscapes.

Diseases affect foraging behaviour

Just as the foraging of bees impacts pathogen susceptibility and transmission, the pathogens can influence the behaviour of foraging bees. For example, Fouks & Lattorff [41] found that bumble bees avoided flowers artificially inoculated with the parasite *C. bombi*. Bacteria in nectar can also deter honey bees and bumble bees from feeding [42],[43]. It remains to be seen how and to what extent bees can detect pathogens while foraging, but these studies suggest bees may be able to reduce exposure to pathogens by altering foraging choices.

On the other hand, once bees are infected, diseases may have a range of effects on foraging behaviour. Schmid-Hempel & Schmid-Hempel [44] were the first to document an association between parasite infections and bee foraging behaviour in the field. *B. pascuorum* workers parasitized by conopid flies were found foraging significantly more often on *Stachys officinalis* than on *Prunella grandiflora* when compared to unparasitized individuals. Additional field studies revealed that conopid and *C. bombi* parasitized bumble bees were less likely to collect pollen for their colony [45],[46]. A number of experimental studies have later found detrimental effects of diseases on various aspects related to the bees' foraging ability. In bumble bees, *C. bombi* reduces foraging speed and the ability to learn floral reward associations and novel flower handling motor patterns [47],[48],[49],[50]. Honey bees infected with *N. ceranae* have reduced homing ability and conduct shorter search flights [51],[52], and honey bees forage less and carry less pollen under increased *Nosema apis* infections [10]. Similarly, DWV infections reduced flight distance and duration in honey bees [53]. Furthermore, DWV and *N. ceranae* infected honey bee workers started foraging at an earlier age [54], potentially through impacts on juvenile hormone levels [55]. An earlier onset of foraging in infected bees could benefit the parasites by increasing horizontal transmission on flowers [54], but direct evidence for an evolved manipulation of pollinator foraging behaviour by parasites is lacking. As a consequence of these various effects, infected bees may be less efficient foragers [10],[45],[56] with negative consequences for individual and colony survival and reproduction.

Bees could also obtain fitness benefits through actively changing their foraging behaviour when infected, in essence self-medicating by preferentially visiting plants with disease ameliorating compounds. Self-medication behaviour has been suggested in other animals [57], including several insect species [58]. For a behaviour to be classified as true self-medication, de Roode et al. [57] outlined five criteria to be fulfilled: 1.) Application or ingestion of a chemical compound or third species; 2.) Initiation of the behaviour by parasite infection; 3.) Increased fitness of the infected individual or its genetic kin by the behaviour; 4.) Costliness of the behaviour to uninfected individuals; 5.) Relevance of the behaviour in natural environments (beyond e.g. artificial diets in the laboratory). For honey bees, increased resin collecting was observed in chalkbrood fungus (*Ascosphaera apis*) challenged hives, and experimentally applying bee-collected resin (propolis) to the interior of the hive reduced chalkbrood infection levels [59]. Stingless bees similarly collect antimicrobial resins [60],[61], but it is unknown if this behaviour is increased or altered by parasite infections. Under laboratory conditions, honey bees preferred honey with higher antimicrobial activity (sunflower honey) over less active honeys under *N. ceranae* infections, and feeding sunflower honey led to a slight reduction in *N. ceranae* spore counts [62]. In the field, Richardson et al. [50] showed that bumble bees naturally infected with *C. bombi* increased foraging for nectar with experimentally increased iridoid glycoside concentrations, compounds that had previously been shown to reduce *Crithidia* infection levels [8]. However, as the association between *C. bombi* infections and iridoid glycoside foraging in this study was correlational, and not based on experimental manipulation, it remains unclear if this behaviour was caused by the infection, or other external factors caused individuals to both be infected and change foraging. In conclusion, these studies suggest that criteria 1, 2, and 5 for self-medication mentioned above have been fulfilled for honey bees, and suggestive evidence has been obtained for bumble bees as well. Crucially, fitness effects, i.e., a fitness benefit of the behaviours under infection and costs to uninfected individuals (criteria 3 & 4) remain to be demonstrated directly. A reduction in parasite numbers (see [8],[62]) may result in fitness benefits, but, as pointed out by de Roode et al. [57], is not a central criterion for demonstrating self-medication. Harmful effects of ingested compounds could negate any benefit of decreased parasite numbers, and conversely, if phytochemicals increase disease tolerance, unaltered parasite counts could still result in host fitness benefits [57]. Experimental tests looking at fitness benefits of foraging behaviour changes under infection are therefore needed to determine if bees are truly self-medicating.

Are diseases reducing pollination services?

Diseases may reduce pollination services by foraging bees in two ways. Firstly, pollinator population declines resulting from diseases could lead directly to reduced pollination services owing to fewer floral visits, negatively affecting food production [2]. Consequently, the global spread of diseases from managed pollinators into wild bee populations is of special concern [6],[63], and better trade regulations are needed to halt the national and international spread of pathogens through the distribution and trade in managed pollinator species [2],[63].

Secondly, an important but poorly understood open question is whether diseased bees intrinsically deliver sub-optimal pollination services. Given that various pathogens have been observed to impair the foraging ability of bees (see discussion above), it would seem likely that pollination services are also altered or impaired. Gillespie & Adler [64], for example, found a negative correlation between

Nosema infection rates in bumble bees at different field sites, and seed set of *Trifolium* and *Solanum* plants. Lach et al. [10] found that honey bees infected with *N. apis* collected less pollen, and infection intensity was negatively correlated with the amount of pollen grains carried on the body of foragers, suggesting a lower efficiency of highly infected workers as pollinators. In contrast, higher *C. bombi* disease loads by bumble bees in urban compared to rural environments did not result in reduced pollination, which instead only depended on the amounts of visits a flower received [65].

Shifts in the floral preferences of infected bees may impact pollination services [66]. For example, *Crithidia* infected bumble bees foraged more and transferred more pollen on *Chelone glabra* flowers with higher iridoid glycoside concentration, compounds previously found to reduce *Crithidia* infections [50]. Potentially, this change in pollinator preference under infection would increase pollination services for plants with higher amounts of nectar iridoid glycosides, but would lower pollination of those plants for which these compounds were at low concentration or absent [50]. Conopid fly infected bumble bees switched more often between plant species while foraging [66], whereas tracheal mite infections increased flower constancy [47]. This suggests that depending on the specific interaction, bee parasites could both increase and decrease within-species pollen transfer between flowers. Certainly, much more detailed experimental work is needed to understand the potential impacts of diseases on pollination services.

Conclusion

Diseases are an important, but still poorly understood factor in bee foraging ecology. Foraging for pollen and nectar exposes bees to a multitude of parasites that are horizontally transmitted via flowers. A better understanding of the epidemiology of disease spread in foraging pollinators and the role of floral traits in influencing transmission is needed if we are to develop effective interventions to reduce the impact of disease on pollinators. The varying nutritional and non-nutritional plant chemistry of pollen and nectar can affect bee diseases, either by directly inhibiting parasites through antimicrobial compounds, or indirectly by influencing host nutritional state, immune function, and the microbiome. Parasites can alter bee foraging behaviour, either through adaptive or non-adaptive impacts of the parasite on bee behaviour, or through bees detecting and avoiding infected flowers. Infected bees in turn could potentially self-medicate by visiting plants with disease-ameliorating pollen and nectar phytochemistry. Both the reduction of pollinator populations and the change in foraging behaviour due to diseases may result in reduced or altered pollination service, highlighting an urgent need to better understand the relation between foraging and bee disease.

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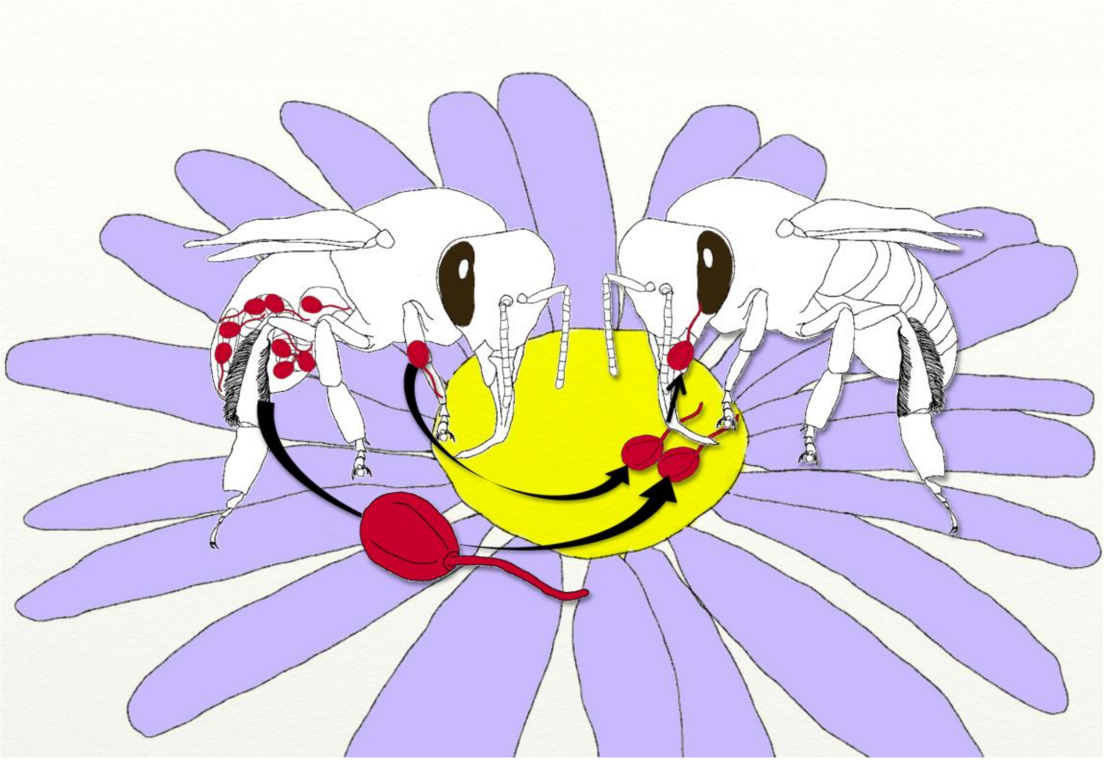

Figure 1: Bees transmit and contract parasites on flowers. Parasites can be excreted by infected foraging bees onto flowers, or vectored on the bees' surface between flowers. Subsequently visiting bees of the same or different species may then ingest parasites while foraging, and become infected.

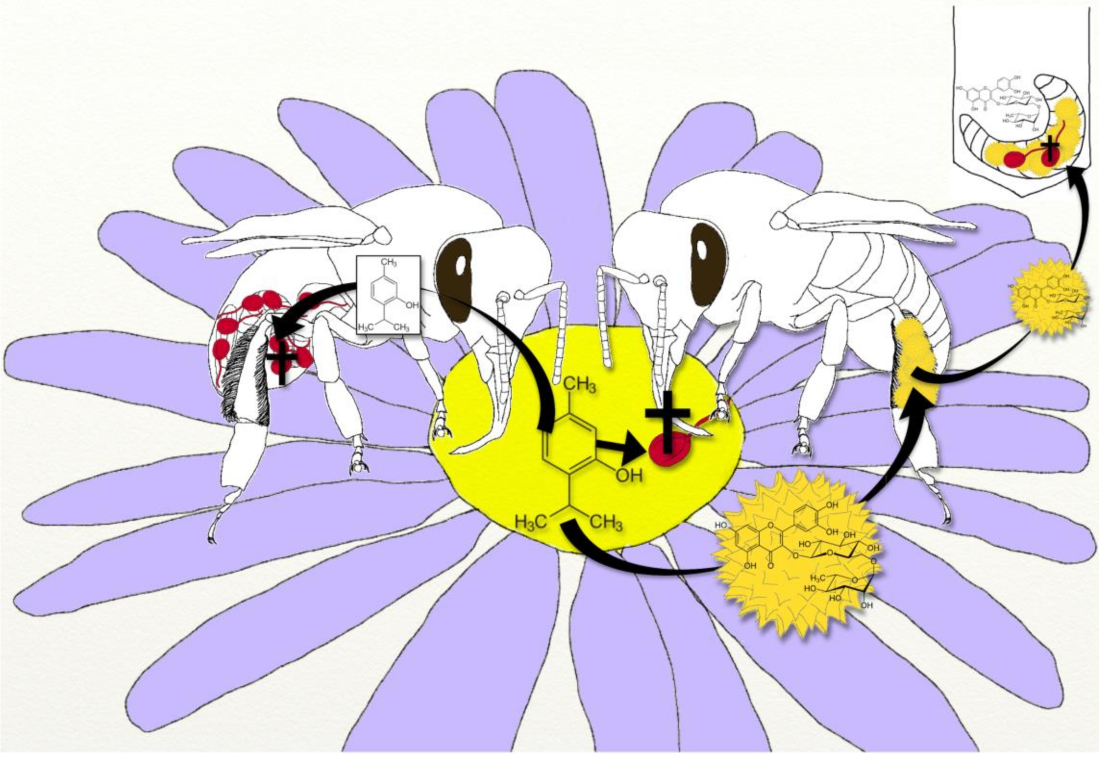

Figure 2: Flower chemistry affects bee diseases. For example, antimicrobial plant metabolites on flowers may kill bee pathogens and reduce floral transmission, and compounds in pollen and nectar can inhibit diseases in the gut of foraging bees or in larvae in the nest.

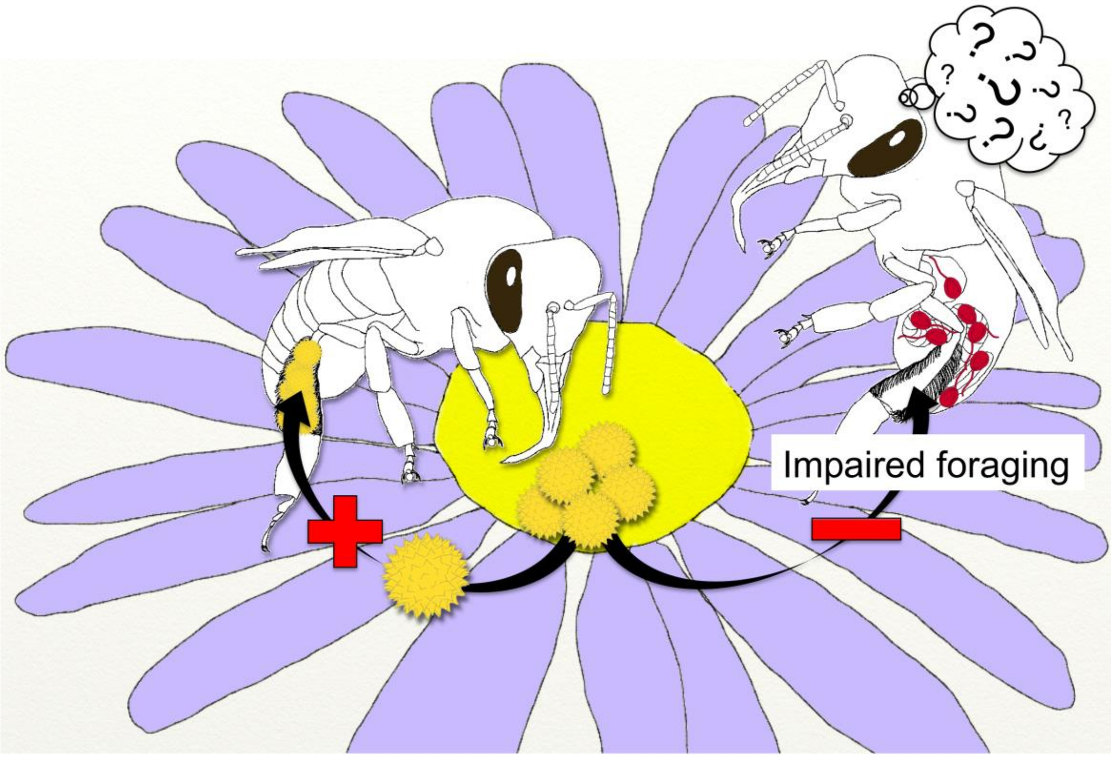

Figure 3: Diseases modify foraging behaviour of bees. Infected bees can be less efficient foragers for example due to less pollen collecting, or a reduced ability to learn floral reward associations and novel flower handling motor patterns.

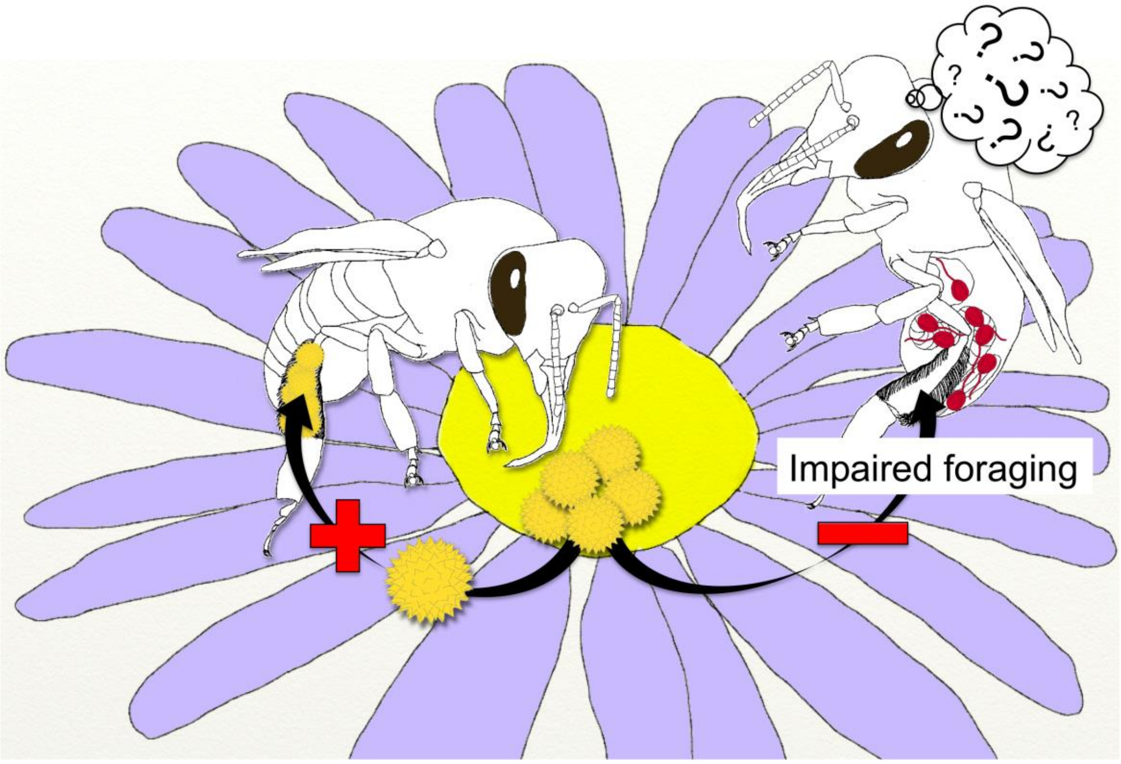

Figure 4: Diseases may reduce pollination services due to a reduction in bee populations or by affecting foraging behaviour, reducing pollen transfer between conspecific plants.