

Social Immunity

Review

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Social insect colonies have evolved collective immune defences against parasites. These ‘social immune systems’ result from the cooperation of the individual group members to combat the increased risk of disease transmission that arises from sociality and group living. In this review we illustrate the pathways that parasites can take to infect a social insect colony and use these pathways as a framework to predict colony defence mechanisms and present the existing evidence. We find that the collective defences can be both prophylactic and activated on demand and consist of behavioural, physiological and organisational adaptations of the colony that prevent parasite entrance, establishment and spread. We discuss the regulation of collective immunity, which requires complex integration of information about both the parasites and the internal status of the insect colony. Our review concludes with an examination of the evolution of social immunity, which is based on the consequences of selection at both the individual and the colony level.

Introduction

Group living has many benefits when compared to a solitary lifestyle. Cooperation can increase the efficiency of brood care, foraging, or anti-predator defences. These benefits are considered as one of the main reasons why, for example, social insects — the ants and termites, some bees and wasps — have become dominant species in many habitats [1]. Living in social groups also has drawbacks, however: infectious diseases can potentially spread more easily between group members, when compared with solitary living individuals [2–4]. The reasons for this are that, firstly, transmission is more likely to happen when individuals live at high densities and have frequent social contact and, secondly, that group members are often close relatives and thus susceptible to the same parasite infections. Hence, it is expected that social groups offer particularly amenable conditions for the spread of infectious diseases [5,6], but they should also have evolved several tactics to counter this threat.

Primates and social insects have, in parallel, evolved sophisticated collective anti-parasite defences, for example, allogrooming behaviour to remove parasites

from group members [4,6–8]. These defences can be prophylactic, such as the intake of tree resin by ants to prevent fungal and bacterial growth on nest material [9]. Other defences are activated on demand, for example, social fever in honeybees, whereby many bees simultaneously raise their body temperature to heat-kill bacteria in their hive [10]. A common factor of these social defences is that they are based on collective action or altruistic behaviours of infected individuals that benefit the colony [11,12]. These defences therefore depend on cooperation of social group members resulting in avoidance, control or elimination of parasitic infections — phenomena that we summarise as parts of a ‘social immune system’.

The individual members of an insect society cooperate to ensure colony growth, survival and reproduction. There is reproductive division of labour such that one or a few individuals, the queens and their mates, produce the colony offspring, while the majority of individuals, the workers, perform tasks such as foraging, nest construction and maintenance, and caring for offspring. The dependence of the colony upon one or a few reproductive individuals means that the fitness of all members of the society is jeopardised when the queen succumbs to a parasitic infection. We would therefore expect that the queen in a social insect colony should be subject to special protection, similar to the germ line or the nerve cells in the brain of a vertebrate body that are subject to an ‘immune privilege’ [13].

Despite differences in the life histories of social insect species, they all share common features of social organisation that make them vulnerable to parasite attack. Members of a colony perform social behaviours that can lend themselves to parasite transmission, for instance, exchange of food by regurgitation, or the transfer of symbionts by anal feeding [14,15]. Social insects generally inhabit spatially and temporally stable nests, in which they maintain long-term stable homeostatic conditions by, for example, active thermoregulation [14,16]. This is particularly the case for ant and termite societies, in which the queens and thus whole colonies can have life spans of up to several decades [1,14,17]. As with long-lived vertebrates, sexual maturity of social insect colonies is reached many months or several years after queen mating; the production of sexual offspring is often possible only after a long growth phase with many sterile worker generations [1]. Most queens are monogamous, whereby they mate with one male at a single event early in their life (see J.J. Boomsma’s review in this issue). Monogamy most probably reduces the risk of disease transmission between mates, although the overall lifestyle of social insects makes them a predictable and amenable environment for parasites.

The scope of this review is to build on previous work outlining the strong parasite-mediated selection pressures on social insects [3,4,18] and to achieve an

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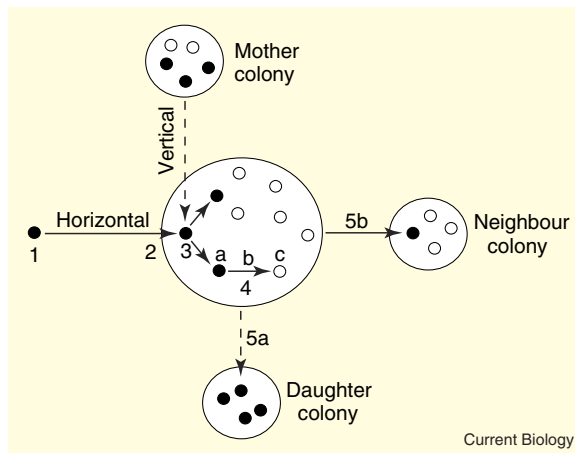


Figure 1. Steps of parasite invasion into social groups.

Schematic diagram of a social group consisting of multiple individuals (small circles), with possible infection pathways between infected (black) and uninfected (white) individuals shown by arrows. Solid lines indicate horizontal transmission into and within a group, and towards neighbouring colonies. Dashed lines indicate vertical transmission from the parental colony to the offspring generation. In order to infect a social insect colony, a parasite has to be (1) picked up from the outside environment (parasite uptake), and (2) introduced to the group (parasite intake). The parasite then has to (3) establish in the internal environment of the social group, and (4) spread among group members. Parasite transmission between two group members depends upon (a) the infectiousness of the infected individual, (b) the contact type and rate between the infected and the uninfected individual, and (c) the susceptibility of the uninfected individual. After infection of the focal group, parasites can be transmitted to other groups either by (5a) vertical or (5b) horizontal transmission routes.

up-to-date appraisal on the mechanisms of collective immunity of social insects, reported in a rising number of studies in recent years. We present a conceptual framework that provides an overview of the subject and allows a new perspective for future studies, in which we hope many of the presented questions and hypotheses will be rigorously tested. We focus on collective defences, and not on individual behavioural repertoires or the individual physiological immune systems of insects as these have been extensively reviewed elsewhere [19,20]. We start this review by describing the steps a parasite must overcome to successfully infect and spread within and between social insect colonies. From this, we derive the expected defence strategies by the social insect host and compare these expectations to the existing evidence. We then illustrate the regulatory mechanisms of social immune systems, their costs and benefits, both at the individual and colony level, and their evolution.

Parasite Invasion into a Social Insect Colony

Damage to social insect colonies is caused by a great variety of parasites, a term we use in a broad sense, to include macroparasites (e.g. helminth worms and arthropods) and microparasites (e.g. fungi, bacteria, viruses and some protozoa) [4], but excluding social insects that parasitise colonies (social parasites [14]). Parasites can either search for and enter the colony

actively, or be picked up and transported into the colony by host individuals. The parasite infections can then be transmitted between individuals. According to the most commonly used notation, ‘vertical’ transmission means transmission from parent to offspring, while ‘horizontal’ transmission is among individuals of the same generation. This distinction is blurred in social insects as parent and offspring live together permanently to form colonies. Therefore, we here refer to ‘horizontal’ as transmission within and between groups (colonies) and to ‘vertical’ as transmission into the next generation, i.e. from mother to daughter colony [4]. In any case, parasite invasion into a colony is a multi-step process: the parasite has to either actively approach or passively be transported to the colony, it has to enter the colony, establish within the nest environment, and spread between group members. It may then exit the colony either horizontally or vertically to new colonies (Figure 1).

Collective Parasite Defence Mechanisms of Social Insects

We suggest that social insects should try to intervene at each of these steps of parasite infection. Host defence performance might be constrained, however, by the colony’s life history and ecology [18,21]. For example, bees forage on flowers whose availability fluctuates temporally and spatially and which therefore cannot be monopolised by a single colony. Unlike ants, for instance, who defend feeding territories around their nest, bees cannot avoid sharing feeding sites with other colonies, despite flowers often being hotspots of infections [22].

In the following paragraphs, we review the examples of social immune defences from the literature, structured into protections against ‘parasite uptake’ from the environment, ‘parasite intake’ into the colony, ‘parasite establishment’ in the social insect nest, and ‘parasite spread’ within colonies, as well as between-colony transmission (Figure 1). For each step, we separate the colony defences into prophylactic measures and activated responses. The presented examples vary in their generality — sometimes they have been documented across taxa, but sometimes examples have only been reported for a single species (for details see Table 1 and references therein). Some mechanisms may also act simultaneously at different steps, but are listed according to the step where we consider them to have greatest impact.

Steps 1 and 2: Reducing Parasite Uptake and Intake

Any new infection of a social group occurs either by vertical transmission from the mother group or by entering the colony from the outside. When parasites actively enter the nest, the risk of an infection depends on whether the nest is open to the external environment, for example, in some wasps and bees and in army ants, or whether the group members are enclosed within a physical construction, as in other bees and wasps, most ants and all termites [18,23–25]. Nest architecture itself may therefore be under selection by parasites [4,26]. When social insects live in enclosed nests, it is the foragers that are most likely to pick

Table 1. Collective immune defences by social insects.

<i>Parasite invasion step/</i>						
Host defence action	Defence mechanism	Response	Mode	Host	Parasite	Reference
1 Uptake from environment						
Reduce exposure risk						
Unshared foraging ranges	Territorial demarcation	Pro	Behav, spatial	Ants, termites	All	[18]
Division of labour	Small proportion of individuals forage	Pro, act	Behav	All	All	[78]
Avoidance behaviour	Avoid direct contact with parasite	Act	Behav	Ants, termites	Fungi, helminths, flies	[27–29,33–35]
	Avoid cannibalizing infected corpses	Act	Behav	Ants, termites	Fungi, helminths	[30–32]
	Guard foraging trails	Pro, act	Morpho, behav	Ants	Flies	[36]
2 Intake into colony						
Bar entrance to infected individual						
Select who enters the nest	Guard nest entrance	Pro, act	Behav	Bees	All	[38,39]
3 Establishment in nest						
Nest hygiene						
Intake of environmental substrate	Collect antimicrobial substances	Pro	Behav	Ants, bees	Bacteria, fungi	[4,9,41]
Use of self-produced chemicals	Metapleural gland secretion	Pro	Behav, physiol	Ants	Bacteria, fungi	[42–45]
	Faecal material	Pro	Physiol	Termites	Fungi, helminths	[47]
	Venom	Pro	Physiol	Wasps	Bacteria, fungi	[48]
Waste management	Corpse removal; separated ‘graveyards’	Pro	Behav, spatial	Ants, bees	All	[27,50–54]
	Garbage removal; separated waste dumps	Pro	Behav, spatial	Ants	All	[56–60]
Keeping parasites local	Cover infectious parasite propagules	Act	Behav	Ants	Fungi	[61–63]
	Social encapsulation (walling) of parasites	Act	Behav, spatial	Bees	Beetles	[64]
4 Spread within colony						
a Reduce infectiousness						
Eliminate parasite propagules	Mechanical removal by grooming	Act	Behav	Ants, wasps, termites	Fungi, helminths	[7,55,67–71]
	Chemical destruction in infrabuccal pockets	Act	Behav, physiol	Ants, wasps	Fungi, helminths	[70,72–76]
b Reduce contact						
Heterogeneous interaction frequency	Behavioural structuring (age & caste)	Pro	Behav	All	All	[4,37]
Social exclusion	Spatial nest compartmentalisation	Pro	Spatial	All	All	[25,26,77–79]
	Indirect interaction with garbage workers	Pro	Behav, spatial	Ants	All	[60]
	Pathogen alarm (vibrational displays)	Act	Behav	Termites	Fungi	[81,82]
Nest relocation	Isolate (walling) infected individuals	Act	Behav, spatial	Termites	Helminths	[27,83,84]
	Remove/cannibalize infected young individuals	Pro, act	Behav, spatial	Bees, termites	Bacteria, fungi	[85–87]
Nest relocation	Abandon infected nest areas	Act	Behav, spatial	Ants, bees	Fungi, helminths, mites	[29,32,67,71,88]
c Reduce susceptibility						
Increase genetic heterogeneity	Multiple mating and/or multiple queens	Pro	Behav, genetic	Ants, bees	All	[91–95]
	Increased recombination rate	Pro	Genetic	Ants, bees	All	[102,103]
Contact immunity	Immunity transfer by social interaction	Act	Behav, physiol	Termites	Fungi	[108]
5 Transmission to other colonies						
Avoid vertical transmission						
Protect queen	No tending by infected workers	Act	Behav	Bees	Microsporidia	[109]
Protect brood	Application of antimicrobial secretions	Pro	Behav, physiol	Ants, bees, wasps	Bacteria, fungi	[51,110]
	Feeding of antimicrobial secretions	Pro	Behav, physiol	Bees	Bacteria, fungi	[111]
	Transgenerational transfer of immunity	Pro, act	Physiol	Bees	Bacteria	[113,114]

Overview of the defence mechanisms employed by social insects to avoid parasite infection. Responses can be prophylactic (Pro) or activated (Act), and employ either a behavioural, genetic, physiological, spatial or morphological defence mode (Behav, Genetic, Physiol, Spatial, Morpho).

up a parasite, as foraging inevitably brings workers into contact with potential pathogens in the external environment. Hence, a valuable first defence would be for foragers to reduce the risk of parasite contraction.

Foraging ants and termites can indeed reduce the peripheral exposure risk by avoiding areas that are rich with parasites [27–29], and by stopping intraspecific cannibalism — an otherwise common behaviour

of social insects — when an individual is infected with a parasite [30–32]. Some ant species ‘hide’ from parasitic phorid flies hovering over the ant foraging trail [33–35], and the smallest caste of leaf-cutting ants hitchhikes on the leaves transported back to the colony by larger workers, probably both to prevent flies from laying their eggs on the large workers and to remove fungal contaminants from the leaves [36]. It is also typically the older — and thus most expendable — individuals who perform the risky task of foraging [4,37].

To prevent parasite intake into the nest, colonies are expected to bar the entrance to parasites or infected incoming foragers. Honeybees indeed have specialised guards that control the nest entrance and, together with the other workers, attack or exclude infected nestmates [38,39]. Selection for this behaviour clearly occurs at the colony level, as it is fatal for the expelled individual.

Step 3: Reducing Establishment of the Parasite in the Nest

If these first protective steps fail, or if parasites enter the colony actively or via vertical transmission, a social insect colony should prevent the parasite from establishing in its nest. Nest hygiene should therefore be extensive, especially so in species with long-lived societies, which may otherwise accumulate high numbers of parasites over time, as well as in species nesting in soil, which itself is rich in parasites [4,18].

Indeed, social insects often disinfect their nest material with antimicrobial substances that are either collected from the environment or self-produced. Like some primates that use the toxic secretions from millipedes to clean their fur [40], bees and ants collect and apply antimicrobial products from the environment to their nest material [4,9,41]. Ants have evolved a unique gland on their mesosoma (thorax), the metapleural gland, which secretes acidic compounds that are effective against both bacteria and fungal spores; the secretion not only protects the ants themselves but is also transferred to the nest material [42–45]. Termites sometimes fumigate their nest with volatile antiseptic chemicals of hitherto unknown origin [46], and enrich their wall-building material with faeces that have antimicrobial properties [47]. Wasps can produce antiseptic substances in their venom glands and on their body surface that stick to the walls of the hibernation sites; these substances are sufficiently long-lasting to protect the next generation of wasps visiting the same hibernation site [48]. In bees, the efficiency of antimicrobial defences themselves seems to increase with the degree of sociality [49].

A considerable risk of infection probably emerges from nestmates that have died from an infection within the colony. It is therefore not surprising that bees, ants and termites quickly remove corpses from their nest and create ‘graveyards’ [27,50–53], a task that is often performed by specialised workers [52,54], sometimes exposing corpses to the UV light of the sun, which rapidly kills emerging fungal spores (E. Groden, personal communication). Some termites bite the legs off the corpses of their nestmates, thus killing infectious parasite stages by desiccating the cadaver [55]. Other

waste, for example food leftovers, is constantly removed from the central nest area and collected at garbage sites located either at the nest periphery or outside the nest, often downhill to prevent rain flushing it back into the nest [27,50–53,56–60], or even dropped into streams (*Atta* ants, S.A.O.A., unpublished data). Waste management thus involves strict spatial separation of clean nest areas and waste dumps.

Parasite infections can be controlled by keeping them local. Ants place fungal spores into piles and cover them with soil [61–63], and Cape honeybees ‘socially encapsulate’ and thereby starve parasitic beetles that enter their nest [64]. These behaviours at the colony level are analogous to the encapsulation response of the individual physiological immune system of insects, which renders an incoming parasite innocuous [19,65].

Step 4: Reducing Parasite Spread between Group Members

Despite precautionary measures, a parasite can become established in the nest; in this case efforts need to be made to prevent the parasite from spreading between group members. The probability of a healthy individual becoming infected is a function of the infectiousness of the infected individual, i.e. the number of infectious propagules it can transfer to its nestmates; its contact rate and the type of interaction it has with non-infected individuals; and the susceptibility of the non-infected individuals. Collective defences are expected to be implemented at any of these three steps and are discussed below.

In terms of reducing infectiousness of the source, examples of mechanical removal and subsequent chemical destruction of the parasite from the body surface of nestmates are found almost universally in social insects. Comparable to the delousing process observed in monkeys [6,8,66], infectious particles such as fungal spores ([7,67,68], and R. Gadagkar personal communication), mites [69] and some helminth worm stages [55,70,71] are groomed off, and allogrooming frequency increases with colony size in ants [4]. In ants and wasps, these infectious propagules are then filtered out in the mouth of the cleaning individual, collected in specific pouches (the infrabuccal pocket), killed by addition of labial gland substances, and finally spat out outside the nest [70,72–76].

Regarding the issue of contact, rates of contact between individuals are limited in many social insect colonies, especially in the large societies of ants and termites, by spatial and behavioural compartmentalisation (Figure 2A). Members of the same age and/or caste perform similar duties within particular compartments, starting with nurse tasks in the centre of the colony followed by colony maintenance duties in the nest periphery, so named centrifugal polyethism [4,37]. As interactions occur mostly within rather than between compartments, infections often stay local within a given compartment (organisational immunity [77]). Most barriers are employed to prevent parasite spread from the entrance point in the outer nest area containing older workers to the inner nest area with the younger nurse workers, the brood and the queen [25,77–79] (Figure 2B,C).

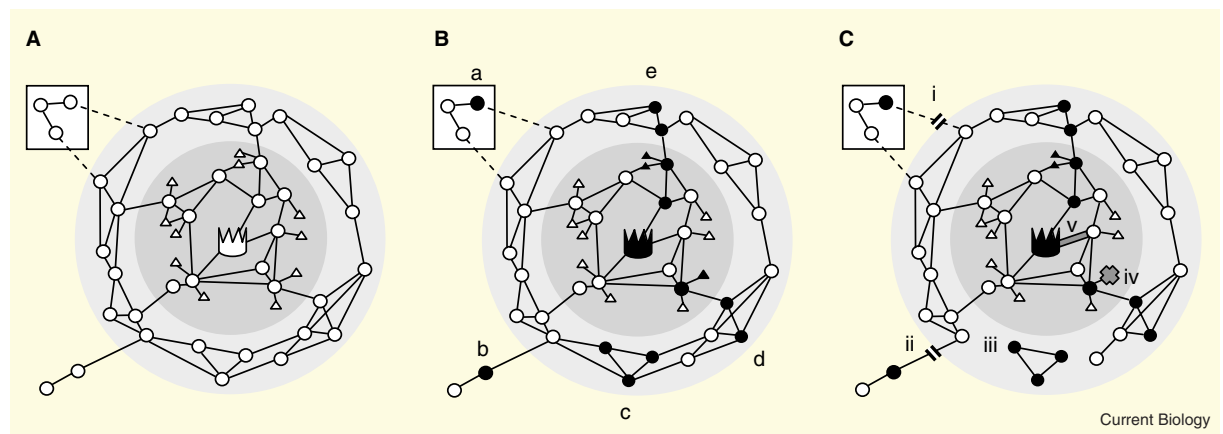


Figure 2. Infections and defence mechanisms of a social insect colony.

(A) Interaction network of a generalised social insect colony. A social insect colony is often organised into spatial and behavioural compartments, between which the frequency of interactions (lines) is lower than within. These compartments consist of workers (dots arranged in groups of concentric circles) of the same age and/or caste that perform similar tasks. In the centre of the nest (dark grey area), the queen (indicated by the crown) and her brood (triangles) are cared for by the young workers. In the periphery (light grey area), older workers perform nest maintenance duties and leave the nest to forage (lower left corner: individuals outside the nest). Disposal of dead bodies and garbage takes place at specific sites at the edge or outside of the nest (upper left corner, rectangle: garbage dump workers only have indirect contact with the main nest, shown by dashed connecting lines).

(B) Fatal and non-critical infections. Incoming parasite infections of the colony can have three levels of severity: lowest level when the infection (infected workers symbolized by black dots) is limited to (a) garbage workers or (b) foragers; intermediate level when the infection reaches and spreads within the peripheral nest area (light grey area) with predominantly old workers (c); highest level when the parasite reaches and spreads within the centre of the nest (dark grey area), where young workers and brood can be infected (d). The infection is fatal when the colony collapses due to depletion of the worker force, or when the queen itself becomes infected (e.g. infection spreads along route e).

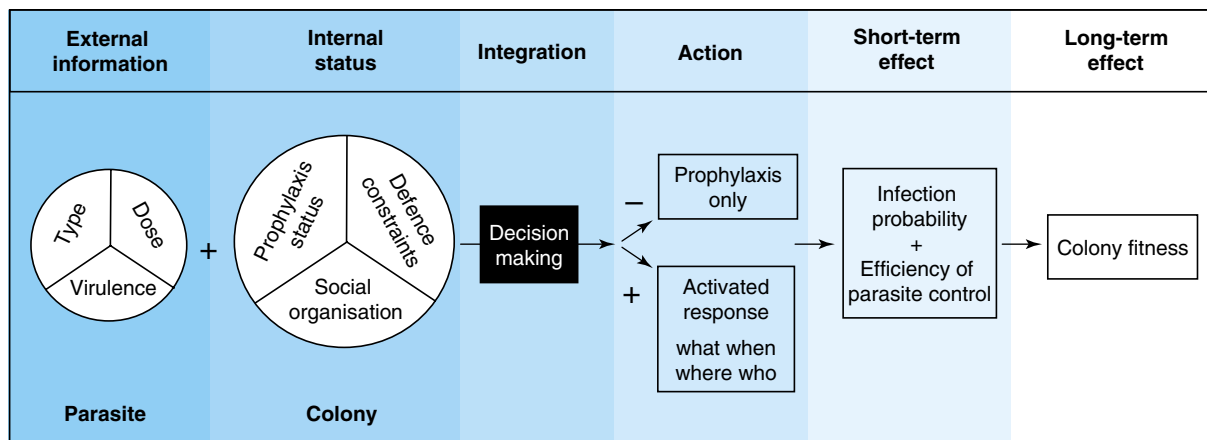
(C) Defence mechanisms to limit spread of an infection. When inside-nest individuals guard colony entrances, garbage dump workers (i) and parasite infected foragers (ii) can be prevented from entering the colony (double line). When the infection has reached the nest (iii), the transmission chain to other individuals within the nest can be broken by reducing social contact (absence of interacting lines). Infected brood items (iv) can be removed from the colony (grey cross). Infected individuals that have a high value for the colony, for example the queen (v), are intensively contacted (thick grey line) by workers that perform hygienic behaviours, such as allogrooming, where infectious propagules are removed from the body surface. The social organisation of the colony can thus be kept flexible and, in principle, adjusted to incoming parasites; this forms an activated response in addition to the prophylactic effect of the nest structure (see (A)).

The more central and cleaner nest areas are protected against incoming parasites from compartments with particularly high infection risk, such as the peripheral garbage heaps. Nest workers interact only indirectly with the workers from the garbage dump as they transport the waste to a caching site, from where it is later picked up by the garbage workers [60] — presumably old workers with a high intrinsic mortality [56]. The queen is especially protected; she is surrounded and intensively cared for by young workers who have never left the protection of the nest [14]. This colony organisation was previously assumed to have evolved to increase the ergonomic efficiency of the colony as a whole [80], but it is becoming increasingly clear that it has important implications for disease transmission [4,25,77,78], because it counteracts the main factor rendering social groups so vulnerable to parasites — spatial and genetic proximity of the members.

In addition to these prophylactic measures, social exclusion is an effective activated response to limit contact rates between infected and non-infected individuals. Termites warn nestmates not to come close to an infected individual by displaying a vibratory pathogen alarm behaviour [81,82]. Furthermore, infected nestmates can be isolated by building walls around them [27,83,84] in a process similar to the production of a granuloma by the immune system in the vertebrate

body [13]. Younger termites, in particular, are sometimes also cannibalized when infected [85], a countermeasure against parasite spread also performed in the honeybee, where specialised workers exterminate infected brood [86,87]. Only when all other measures are ineffective, and a major parasite outbreak occurs, would healthy individuals completely abandon the nest, and move to a new location leaving infected individuals behind either in the old nest or whilst on the move [4,29,32,67,71,88].

Finally, in terms of the issue of host susceptibility, a potent individual immune system or low susceptibility to the parasite can prevent parasite transmission despite contact with the infected individual. As members of insect societies are typically genetically highly similar, it is assumed that they are susceptible to similar parasites. One prophylactic defence strategy would therefore be to increase the genetic diversity within colonies [89,90]. Indeed, social insect colonies with multiple versus single mating of the queen, or brood from multiple versus a single queen in the colony suffer less from parasites than colonies consisting of group members with higher relatedness [91–95]. This might be facilitated through an observed genetic predisposition of offspring of different patriline to develop into different castes [96] combined with a caste-specific immune repertoire [97,98]. Negative effects of low genetic



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Figure 3. Regulation of the social immune response.

The response of a social insect colony (large circle) to a parasite (small circle) should take into account both the external information about the parasite (e.g. its type, dose and virulence) and internal information on the status of the colony. The colony state is determined by the social organisation of the colony members, the degree of prophylactic defence, and also by potential constraints on anti-parasite defence, such as limited recognition or handling capacities. Details of how the decision-making process occurs (black box) are still not understood; the outcome is either (-) no action, i.e. the colony relies solely on its prophylactic defence, or (+) take action, i.e. an activated response is triggered. In the short term, the outcome of these actions affects the infection risk and efficiency of parasite control of the colony, and in the long term, colony fitness. Natural selection can then lead to the evolution of e.g. an optimised colony structure or a better parasite recognition ability, and lastly can shape the decision-making process itself.

diversity are also seen in studies finding that inbreeding might increase parasite loads [99] (but see also [100,101]). Comparative studies on the recombination rates of social and non-social insects indicate a higher recombination rate in the social insects [102,103], which also increases genetic heterogeneity. It is worth noting, however, that the effects of genetic diversity are not always so simple [104] and that a high genetic heterogeneity, whilst reducing the damage of single parasite infections, can at the same time increase the susceptibility of the colony to a greater range of parasites, which is why this strategy might not be beneficial under all conditions [105–107]. Susceptibility of nestmates may additionally be reduced by the ‘social transfer of immunity’ found in some termites, where social contact with an infected individual promotes immunity of previously naïve nestmates [108].

Step 5: Reducing Vertical and Horizontal Parasite Transmission

Once a parasite has proliferated within a colony, it can be passed on to other groups, be they independent neighbouring colonies or daughter colonies. Vertical transmission to daughter colonies can occur when reproducing queens lay infected brood, or when the daughter queens or accompanying workers, in the case of nest budding, acquire an infection by either horizontal or vertical transmission before leaving the parental colony. Although there may not be strong selection against the avoidance of horizontal between-colony infections, selection pressures to prevent vertical transmission to daughter colonies should be strong, because the colony fitness depends heavily on the production of successful offspring colonies. Therefore, infected honeybee workers that stop tending the queen [109] and wasps that protect their

juvenile stages by rearing them in brood cells impregnated with antimicrobial secretions [110] could be interpreted as strategies to avoid infection of daughter colonies. Whilst laying eggs, ant queens sometimes coat their eggs with venom, and workers can spray venom over the brood, which apparently reduces fungal infections [51]. Protective substances can also be directly fed to the brood, such as royalisin and other antimicrobial peptides in honey in the honeybee [111]. In addition, a ‘transgenerational transfer of immunity’ to the offspring, similar to that found in other organisms [112], is known for social insects [113,114]. By contrast, avoidance of horizontal infection of neighbouring colonies is rarely expected, only if neighbours are related and/or if this might directly reduce the re-infection risk of their own colony.

Regulation of Collective Immune Defences

As illustrated above, a profusion of defence strategies is available to a social insect colony, and it is important to find the appropriate response, given both the external parasite pressure and the internal status of the colony (Figure 3). The colony members will not only have to decide which defence mechanism to employ, but whether or not to start a response at all, when and where to start it, and who should be responsible for the defence mechanism and who should be protected by it. When several individuals are infected and help cannot immediately be given to everyone, a ‘triage’ may be required involving some knowledge about the differences of the future value of the respective individuals, so that the queen, for example, would receive preferential treatment when compared with a garbage worker.

To make these decisions and to find the appropriate response — as both an over-reaction and an

under-reaction will be costly [13,115] — the colony members have to simultaneously take into account external information about the amount and virulence of the parasite, as well as information about the internal status of the colony, for example, how many and which individuals are exposed, infected, or immune, and how efficient the prophylactic defence is against this particular parasite. In this respect, the challenges facing a social insect colony are similar to other complex regulatory systems, for example, brains and the acquired immune systems of vertebrates. For all of these systems we lack a clear understanding of how the individual constituent parts interact with one another in the decision-making process.

We propose that the study of social immune systems can contribute some understanding of how complex regulatory systems are organized in general. We suggest that social insect societies are appropriate study systems to address this question, because these societies are easily approachable experimentally (as their colonial organisation allows us to observe communication between individuals and to manipulate group compositions) and because social insects are a naturally diverse group, in which social organisation ranges from small and apparently simple colonies to large and complex societies [1]. Insect societies are therefore particularly amenable to a comparative approach.

Consequences and Evolution of Collective Defences

Whereas several studies have assessed the costs of individual immune defences [116,117] and the trade-offs between immunity and other life-history parameters within individuals [118,119] in social insects, comparable studies on the cost of collective defence are much more difficult to perform and thus noticeably absent from the literature, even if one can make the basic assumption that raising a collective immune response should be both energetically costly and time consuming for the colony [120]. On the other hand, the potential benefits to infected individuals of being reared within their social groups have been assessed as being typically high [7,55,67]. Sometimes, however, infected individuals are not cared for but instead killed or excluded from the group. These seemingly drastic measures may enhance colony survival, and resemble what happens in vertebrates during viral infection: infected cells and their uninfected neighbouring cells are killed by natural killer cells to prevent the spread of a virus [13]. Overall, the performance of collective defences has apparent benefits for the colony, even if some hygienic behaviours might under some conditions also increase parasite transmission to previously uninfected group members [30,121,122].

When considering the evolution of social immunity with its multi-layered cost-benefit calculations at both the individual and colony level, it is important to note that kin selection and group selection models are equivalent in the colonies of social insects as they consist of highly related individuals (for details see J.J. Boomsma's review in this issue). The defence mechanisms of social immunity might have originally evolved within other life history contexts, only later

gaining function in parasite defence. Vice versa, immune defence mechanisms in social insects may also become co-opted for different functions; for example, chemical compounds that have evolved for parasite defence may secondarily be used for communication [123]. Collective defences in social insect colonies might have also in part evolved from solitary anti-parasite defences, but it is important to recognize that the collective defences are group efforts and thereby differ from the upregulation of individual immune defences observed in individuals of solitary species under crowding [124]. High investment into group level defences might even co-occur with low investment into individual immune systems, if social immunity is very effective and less costly than maintaining individual immunity. Some potential support for this idea is provided by a recent analysis of the honeybee genome revealing that honeybees apparently lack several immune genes present in non-social insects [125], but more species need to be studied to test the generality of this finding.

Conclusions and Outlook

We conclude that insect societies have evolved highly complex social immune systems that form functional barriers at every step of parasite invasion by a combination of prophylactic and activated responses as well as behavioural, physiological and spatial mechanisms. The available literature is biased towards economically important social insects and their parasites, for example parasites of domesticated species like the honeybee or parasites used as pest control treatment against invasive ants and termites. This bias towards the highly complex social insect societies leaves open the question of whether the collective defences of smaller societies such as wasps are equally sophisticated or of a simpler nature [18].

The theoretically expected strategies still need further exploration; for example, when would there be selection for altruistic suicide of an infected individual or what would be the effects of herd immunity by a sufficiently high proportion of resistant workers [126] or even an active shield of immune nestmates around the infected individual? Future comparative studies, relating collective defence strategies to habitat or nest location (for example, [127]), will furthermore help to understand how different selection regimes have shaped collective immunity and different social organisations. A better understanding of social immunity might even lead to the reassessment of the evolution of host behaviours that have previously been suggested to be the result of parasite manipulation, such as infected individuals leaving the nest.

Overall, we suggest that the major risk of group living — representation of a homogeneous target of many frequently interacting and genetically similar individuals — is often limited by spatial and behavioural compartmentalisation of the colony, or genetically by the evolution of multiple mating for example. The strategies are remarkably diverse and even seem to be conflicting in some cases: infected individuals either receive a lot of care, or on the contrary, might be killed off. To date, the regulatory mechanisms underlying social immune systems remain unexplored.

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