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Organisational immunity in social insects

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Selection for disease control is believed to have contributed to shape the organisation of insect societies — leading to interaction patterns that mitigate disease transmission risk within colonies, conferring them 'organisational immunity'. Recent studies combining epidemiological models with social network analysis have identified general properties of interaction networks that may hinder propagation of infection within groups. These can be prophylactic and/or induced upon pathogen exposure. Here we review empirical evidence for these two types of organisational immunity in social insects and describe the individual-level behaviours that underlie it. We highlight areas requiring further investigation, and emphasise the need for tighter links between theory and empirical research and between individual-level and collective-level analyses.

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Introduction

Disease transmission in animal societies is believed to depend greatly on the structure and dynamics of their social interaction networks, which represent pathways over which infectious propagules can be transmitted [1,2••,3••,4–18]. The effects of interaction patterns on epidemic dynamics have been thoroughly investigated in theoretical studies (Box 1). However, empirical validation of their predictions has been scarce due to the difficulty of obtaining comprehensive datasets on interactions and disease transmission in large animal groups. Studying experimentally amenable model systems such as colonies of social insects (social bees and wasps, all ants and termites) may help overcome this constraint and gain new insights on how social organisation influences disease dynamics and epidemic outcomes in social groups (Figure 1).

Social insects are particularly vulnerable to disease because the frequent and close interactions among genetically related colony members favour pathogen transmission. In addition to their individual immune system, they have evolved collective disease defences known as 'social immunity' [14]. Social immunity is expressed through a variety of sanitary behaviours and the use of antimicrobials, which reduce the infection risk and pathogen load of exposed individuals [14,19–21]. Moreover, the organisation of insect societies may also contribute to social immunity [14–18]. In particular, certain patterns of interactions among group members have been claimed to limit pathogen spread at the colony-level and decrease the infection risk of valuable individuals, such as the queen, brood or young workers, providing a form of 'organisational immunity' [16]. Interaction patterns that reduce disease risk may be constitutively expressed in healthy colonies and play a preventative or prophylactic role, or be induced upon contact with pathogens, through behavioural changes that further reduce transmission risk from infectious to healthy individuals [14].

Testing the organisational immunity hypothesis in social insects has been facilitated by the recent development of data collection techniques and analytical approaches, such as high-throughput automated tracking of individuals within colonies (reviewed in [3••,22•]) and the application of social network theory to epidemiology and behavioural ecology [4,23]. However, unequivocal testing remains challenging because it is experimentally difficult to: (i) manipulate colony-level interaction patterns without modifying other potentially epidemic-relevant parameters such as colony size, hunger levels or health status; (ii) track the propagation of pathogens and/or non-pathogenic proxies in real time and thus (iii) establish a clear causal relationship between the structure of interaction networks and transmission dynamics; and (iv) understand how individual behaviour influences collective dynamics. Empirical work has therefore often been limited to partially addressing different aspects of organisational immunity (Table 1). Here we present an overview of the existing empirical support for organisational immunity in social insects and the individual behavioural rules that are believed to underlie it. We attempt to elucidate general concepts of organisational immunity and highlight areas deserving further investigation.

Evidence for organisational immunity in social insects

Interaction patterns and colony-level disease spread

Explicit simulations of disease spread over simulated interaction networks have proven a powerful approach to formally investigate the role of social organisation in disease dynamics. These analyses revealed that the structural properties of interaction networks (e.g. degree distribution, clustering coefficient, and community structure) have a crucial influence on transmission dynamics and final epidemic size ([4–7,10,24•]; detailed in Box 1). Similarly, the extent to which disease spreads within groups depends on the temporal dynamics of interactions among individuals, such as the time ordering and temporal overlap of interactions, or the existence of repeated contacts [13,25]. Empirical studies that combined social network analysis with the physical tracking of non-pathogenic proxies spreading through colonies (e.g. microbeads [16,26] or food [27,28]; Table 1) confirmed that social network properties influence transmission in social insects. Indeed, changes in network structure induced by experimentally manipulating food quality or foraging motivation led to predicted changes in transmission patterns in the honeybee *Apis mellifera* [16,26,27] and the ant *Temnothorax albipennis* [28]. In particular, non-pathogenic proxies spread less broadly and less evenly over networks of lower density [16,26–28] and/or increased clustering [16,26], and spread faster and more uniformly in groups with higher spatial mixing among individuals and higher temporal overlap of interactions [28].

It remains unproven, however, whether the structure of interaction networks naturally observed in social insects really contributes to limit disease spread through the colony (i.e. whether it provides prophylactic organisational immunity). Most support for this hypothesis comes from agent-based models showing that social heterogeneities, arising for example from division of labour or differences in life history and disease susceptibility among different types of individuals, help contain disease in social insect colonies [15,17,29]. Social heterogeneities result in interaction heterogeneities, that is, interactions are not distributed uniformly within the colony, but some pairs of workers interact more frequently than others. This leads to the formation of partially isolated groups of individuals, or communities, with reduced transmission rates across groups [14,15,29]. Empirical evidence that social networks do contribute to mitigate disease risk is however still scarce. Testing the effect of interaction heterogeneities on disease spread can be achieved by comparing the transmission properties of real social insect networks with appropriate null models (Table 1). So far, most such studies have focused on information flow over networks [2••,30••,31••]; however, their outcome can be reinterpreted in terms of disease transmission because they use similar modelling approaches to those investigating pathogen spread [32•]. Analysis of time-ordered contact networks in the ant *Temnothorax rugatulus* revealed slower colony-level propagation compared to a diffusion null model [30••], which could lend support to the organisational immunity hypothesis. By contrast, the interaction skew observed among *Pogonomyrmex barbatus* ant workers near the nest entrance was shown to enhance information flow compared to uniform interaction null models [31••]. These examples illustrate the difficulty of determining the adaptive value of interaction patterns observed in social insect colonies. These have indeed evolved under conflicting selection pressures and likely represent a compromise between the need to reduce disease spread on one hand, and to ensure high work output, fast information flow, and colony resilience on the other hand [3••,15,31••]. Studies that explicitly address the differences in transmission properties between information and pathogens will be crucial to better understand the significance of interaction networks in terms of disease control and colony efficiency.

It also remains unproven whether social insects can alter their interaction patterns upon encountering pathogens to further reduce disease propagation (i.e. whether they show induced organisational immunity). So far there has been only one investigation of group-level transmission dynamics in pathogen-exposed colonies [33], and this study lacked comparison with non-exposed control colonies (Table 1). Theory may help generate testable predictions for future empirical studies of induced organisational immunity (Box 1).

Interaction patterns and individual probability of infection

The fitness consequences of infection in social insects depend not only on overall disease incidence, but also on the identity of individuals contracting the disease. For example, losing a queen is more costly to the colony than losing workers. Similarly, losing young workers is more costly than losing older workers, which have shorter expected life expectancy [34]. Highly valuable individuals appear to be protected against disease via interaction heterogeneities, which result in their social isolation from 'high-risk' individuals (i.e. old workers that have a high chance of having encountered pathogens and perform high disease-risk tasks such as foraging [2••], waste management [35,36], undertaking [37] and hygienic behaviour [21]). There is good evidence that the queen and young workers are protected from potentially harmful external agents. Studies tracking the propagation of non-pathogenic proxies through honeybee colonies indeed revealed lower prevalence and intensity in young workers [15,27] and the queen [27] than in older workers. Moreover, time-ordered analysis of trophallaxis (i.e. social food sharing) networks in the ant *Camponotus pennsylvanicus* showed that there is a long delay between foragers introducing new food into the colony and the queen receiving it, which was suggested

to decrease the risk of transmission of external pathogens to the queen [32•]. In honeybees, the protection of the queen and young workers was assumed to derive from the consistently observed biases towards within-age-group interactions [16,26,38,39••], which lead to between-age-group compartmentalisation [39••]. This hypothesis is supported by a study of the social interaction networks in the ant *Camponotus fellah*. Colonies of this species appear to be loosely organised into three groups, or communities, showing more frequent within-group than between-group interactions: the queen and young nurses, middle-aged workers performing nest maintenance and cleaning, and old foragers [2••]. Simulation of propagation over these empirical networks revealed faster information spread within than between communities when the source originated from the foragers [2••]. These results indicate that age-and-task interaction biases play a crucial role in isolating the queen and young workers from the outside environment. Interaction heterogeneities leading to colony compartmentalisation into groups that differ in their value for the colony and/or in their disease exposure risk are likely to be widespread in the organisation of insect societies. For example, workers performing high disease-risk tasks are usually highly specialised and have few interactions with other workers [35–37,40], which leads to their social isolation.

Regardless of the identity of their interaction partners, individuals could also be at higher or lower risk of infection depending on their position within the interaction network. For example, individuals with a high number of interaction partners, or individuals that occupy an intermediary 'bridge' position between communities, may be more vulnerable than isolated individuals. In network analysis, this can be formally quantified via measures of node centrality (e.g. degree or betweenness; Box 1). The only empirical study that specifically tested for a correlation between the degree centrality of individuals and their infection rate did not find evidence for this hypothesis [33], but that study involved very small, incipient colonies. Because colony size limits the complexity of colony organisation [41], these may have been too small for organisational immunity to develop.

Box 1 Modelling social interactions and disease transmission

Most epidemic models classify individuals in a group according to their disease state (e.g. susceptible-infectious in the simplest SI model). This type of models traditionally assumes random mixing of individuals, that is, every individual interacts with any other with the same probability [1]. Yet, the contact patterns observed in social groups, in particular social insect societies [2••], deviate widely from the assumption of random mixing. Recent studies have therefore focused on simulating epidemic spread over networks, which explicitly describe all interactions. In such an approach, an edge between two nodes represents an interaction between two individuals (e.g. grooming, trophallaxis), potentially leading to disease transmission. At every time-step, disease may 'travel' — with a given probability — from an infectious node to a neighbouring susceptible node, making it infectious. Other studies have defined networks in different ways (e.g. nodes as areas and weighted edges as the number of individuals moving across them [3••]).

Compared to a 'random mixing' model, an individual in a network has a relatively small number of susceptible contacts, which quickly become infected. This local depletion of susceptible contacts is present in all networks and, to different extents, leads to reduced early growth rate and smaller final epidemic sizes [4]. The following network features further influence epidemic outcome.

Density. *Proportion of all possible edges that are actually present* (Figure B1a). In the simplest scenario, a random network where all nodes have the same number of edges (i.e. they have the same degree), an increased density will ensure faster spread [5]. This trend can be countered by other structural features of a network.

Degree heterogeneity (D). *Variance in degree of nodes* (Figure B1a,b). In a random network where nodes have different numbers of edges, diffusion (e.g. of a pathogen) accelerates with increasing heterogeneity. In these networks, disease cascades from high-degree nodes ('hubs') to low-degree nodes, which is why hubs have been a target for vaccination efforts [5], although, influential nodes or 'super-spreaders' (i.e. individuals that have a disproportionately high likelihood of spreading the disease to others) are not necessarily high-degree nodes [6].

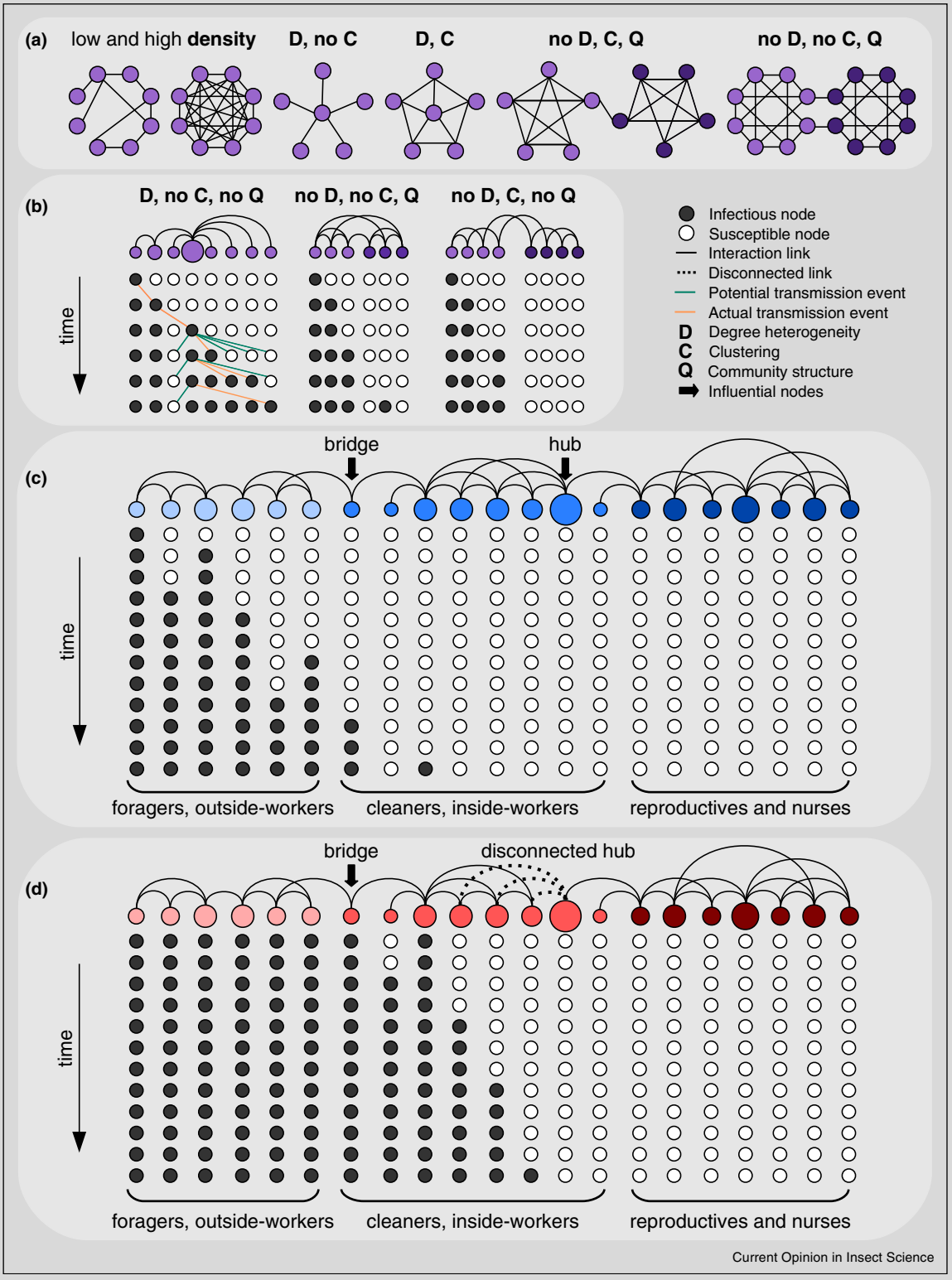
Clustering. *Propensity of two neighbours of a given node to also be directly linked to each other* (Figure B1a,b). Clustering coefficient (C) is a common measure to describe clustering. Epidemic simulations over networks with a large C show reduced initial growth rate and smaller epidemic sizes, given a fixed global transmission rate [7,8]. Nevertheless, the hampering effect of clustering on initial growth rate can be counterbalanced by increasing the transmission rate parameter, in which case, larger C results in larger final epidemic sizes [8].

Community structure. *A network is said to show community structure if it is a loosely connected set of tightly connected nodes* (Figure B1a,b). Modularity **(Q)** is a commonly used measure of community structure. Greater Q can lead to a smaller final epidemic size and peak prevalence [9]. Interestingly, it can also increase the total duration of the epidemic [10]. By contrast, in traffic-driven epidemic models, community structure accelerates the speed of epidemic propagation [11].

Characterising social insect interaction networks for the above-mentioned structural features, and measuring their effect on disease spread over networks will lay a strong basis for the organisational immunity hypothesis (Figure B1c,d). It will be particularly interesting to determine the effect of the network structure on the 'vulnerability' (i.e. the probability that a node is reached by a pathogen, if the outbreak starts from a random node) and 'criticality' (i.e. the reduction in epidemic size if a given node is removed from the network by vaccination or isolation) of particular individuals in the network [12] (Figure B1c,d).

Static networks with undirected links have provided useful and fruitful models to understand epidemics. However, the relaxation of both conditions has also been explored. Directed links can be important in cases where pathogen transmission is linked to inherently non-symmetric process, such as food sharing. Furthermore, the field of temporal (or dynamic) networks has emerged to include more realistic time-ordered interactions where the sequence of interactions dictates the paths of disease. Lastly, networks that change in time can change adaptively. The latest studies of epidemiology examine social networks in which nodes can disconnect links as soon as they detect the infection [13].

Figure B1



Network properties and disease spread. **(a)** Structural features relevant in epidemic spread. **(b)**–**(d)** Epidemic propagation in networks showing different structural features. Nodes coloured according to their disease state: a pathogen may travel, stochastically, from infectious nodes (black circles) to neighbouring susceptible nodes (white circles). The network is a time-aggregate of all interactions which could lead to transmission (interaction link), yet at each time point, transmission events are possible only from currently infectious to currently susceptible nodes. An explicit epidemic sequence is exemplified (orange lines for actual, turquoise lines for potential transmission events, respectively); notice the fluctuation in

From individual behaviour to interaction patterns

Interaction heterogeneities mediating prophylactic organisational immunity arise from three main factors (Figure 1): spatial organisation of the colony, temporal activity patterns and behavioural modulation of interactions among workers. The effects of spatial segregation on colony compartmentalisation are particularly well established, whereas temporal and interaction modulation effects have been less well studied. Pathogen-induced changes in space use and pairwise interactions have usually been interpreted as adaptive host responses that help contain disease. However, one should note that they could also correspond to side effects of disease and/or immune responses, or even to pathogen manipulation. Whereas studies using non-pathogenic proxies partially bypass these difficulties [42•,43,44,45,46,47•], more investigations of real pathogens attempting to discriminate between these three potential underlying causes [48] are required to properly test the induced organisational immunity hypothesis.

Spatial segregation

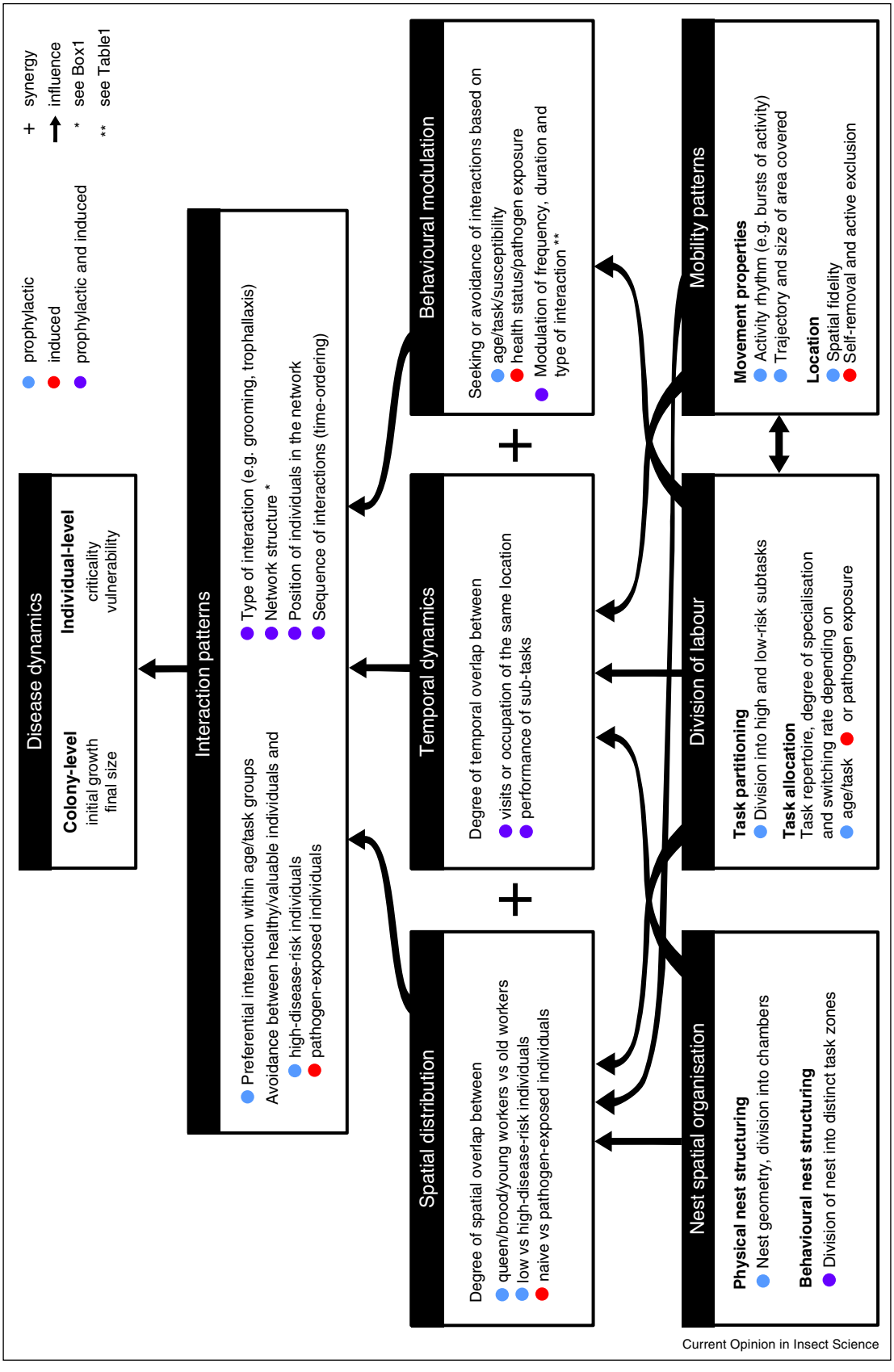
Spatial heterogeneities arising from division of labour in social insect colonies are a crucial underlying factor of prophylactic organisational immunity. Space-embedded epidemiological models involving explicit spatial constraints indeed showed that spatial structuring *per se* can limit disease spread [49–52]. In addition, empirical studies of *Temnothorax* ant networks suggested that spatial fidelity of individuals hinders the propagation of spreading agents through the colony, such as food or pathogens, because it results in spatial segregation [28,30••]. The effect of spatial segregation on disease spread can be explained because space use strongly influences interaction patterns at both individual and collective levels. For example, ants moving over small areas interact infrequently and form long-lasting associations with a small number of social partners only, whereas mobile individuals have a denser, broader and more homogeneous interaction spectrum [31••,53]. Although the implication of these findings for disease risk was not considered formally, this suggests that the movement characteristics of individuals might affect their likelihood of being exposed to disease. Moreover, in the ant *C. fellah* and in the honeybee, within-colony interaction heterogeneities were shown to emerge solely as the consequence of spatial segregation between groups of individuals [2••,39••]. Spatial segregation thus appears to be a crucial underlying cause of the social compartmentalisation of the colony into communities, which is believed to greatly contribute to prophylactic organisational immunity (Section 'Evidence for organisational immunity in social insects').

Spatial segregation is common within social insect colonies, as individuals do not occupy space uniformly, but spend most of their time in small, distinct spatial fidelity zones [2••,26,54–57]. Spatial segregation is mainly explained by the strong division of labour characterising most insect societies combined with the existence of spatially distinct nest areas where different tasks are performed [2••,39••,55,56], and it can be reinforced by specific nest geometries [50]. Division of labour and nest spatial structuring contribute to prophylactic organisational immunity in two main aspects. First, they decrease the spatial overlap between age groups, differing both in their value for the colony and in their potential for infection. This occurs as a direct consequence of age polyethism: as they age, workers in many social insect species shift from inside tasks distant from the nest entrance, such as brood and queen care, to peripheral tasks like food processing and nest maintenance, eventually performing outside-nest tasks at the end of their lives [2••,38,55]. Second, they ensure the spatial isolation of workers performing high disease risk tasks. For example, in the leaf-cutter ant *Atta colombica*, waste is kept in separate nest chambers in which waste heap workers are confined, decreasing their rate of contacts with fungus garden workers [35].

Since spatial heterogeneities can lead to prophylactic organisational immunity, induced organisational immunity could be mediated by an increase in spatial segregation between potentially infectious and healthy individuals. Such spatial changes have been repeatedly shown to occur upon pathogen exposure, although their effect on colony-level disease spread has not been studied formally. In many cases, pathogen exposure leads to the complete exclusion of exposed individuals. For example, ants exposed to an entomopathogenic fungus voluntarily leave the nest, a behaviour known as 'self-removal' [48,58,59••] (see [58,60] for a general effect of health condition on self-removal). Moreover, diseased individuals

the number of possible transmission events (orange + turquoise lines). (b) Degree heterogeneity can lead to the existence of 'super-spreaders' which, once infectious, quickly spread the pathogen to a large portion of the group. Clustering leads to susceptible depletion, which slows down spreading. Community structure can confine epidemics inside a single community. (c) Example propagation over a network with three distinct communities and containing high-degree nodes, illustrating a possible configuration of an insect colony; the epidemic is constrained to the outermost community of foragers for a long time, making it unlikely that the high-valued individuals of the inner-most community become infectious. (d) Example propagation over the same network later in time, illustrating adaptive edge modification, where inside-nest workers cut their links to the community hub (dotted line), when one of their neighbours becomes infectious. Notice that it would also make sense to target a community bridge. In all networks, colour is according to relevance in prophylactic (blue), induced (red), or both types of organisational immunity (purple). Shading marks different communities, and node size signifies degree.

Figure 1


prophylactic
induced
prophylactic and induced
+ synergy
influence
* see Box1
** see Table1
Disease dynamics
Colony-level
initial growth
final size
Individual-level
criticality
vulnerability
Interaction patterns
Preferential interaction within age/task groups
Avoidance between healthy/valuable individuals and
high-disease-risk individuals
pathogen-exposed individuals
Type of interaction (e.g. grooming, trophallaxis)
Network structure *
Position of individuals in the network
Sequence of interactions (time-ordering)
Behavioural modulation
Seeking or avoidance of interactions based on
age/task/susceptibility
health status/pathogen exposure
Modulation of frequency, duration and
type of interaction **
Temporal dynamics
Degree of temporal overlap between
visits or occupation of the same location
performance of sub-tasks
Spatial distribution
Degree of spatial overlap between
queen/brood/young workers vs old workers
low vs high-disease-risk individuals
naive vs pathogen-exposed individuals
Division of labour
Task partitioning
Division into high and low-risk subtasks
Task allocation
Task repertoire, degree of specialisation
and switching rate depending on
age/task or pathogen exposure
Mobility patterns
Movement properties
Activity rhythm (e.g. bursts of activity)
Trajectory and size of area covered
Location
Spatial fidelity
Self-removal and active exclusion
Nest spatial organisation
Physical nest structuring
Nest geometry, division into chambers
Behavioural nest structuring
Division of nest into distinct task zones
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are sometimes actively excluded by their nestmates: in termites, nematode-infected individuals are walled in [14], whereas in the honeybee, infected workers are declined entrance [14] or dragged out of the hive [61•]. Certain species have evolved devoted communication channels to respond to pathogen threat: upon contact with contaminated substrates, workers of the termite *Zootermopsis angusticollis* produce vibrational alarm signals triggering escape behaviour in unexposed nestmates [62]. In other cases, spatial segregation is increased indirectly, via a decrease in mobility [43] or changes in the task repertoire of exposed workers. For example, *Pogonomyrmex barbatus* ants are more likely to perform waste work if they interact more frequently with waste workers [63]. In ants and honeybees, workers subjected to pathogen exposure or immune stimulation stop tending the queen and brood [42•,48,59••,64] and switch to outdoor tasks like foraging or defence against intruders [34,42•,59••,64,65••,66•], thereby increasing their distance to valuable individuals. In honeybees infected by microsporidians of the genus *Nosema*, these behavioural changes are concomitant with physiological changes, including an above normal increase in production of Ethyl Oleate (EO) by infected workers [65••,67]. EO is a pheromone that inhibits the behavioural maturation of in-hive workers [68]. This leads to the testable hypothesis that in addition to becoming early foragers [34,64,65••,66•], *Nosema*-infected workers may also delay the onset of foraging in their healthy nestmates. Such social readjustment could be beneficial for infected colonies, because it would both decrease the spatial overlap of healthy with infected workers and delay the draining of the nursing force induced by *Nosema* infection [69].

Temporal heterogeneities

Theory shows that the temporal dynamics of interactions influence disease spread (Section 'Interaction patterns and colony-level disease spread'). Because they contribute to shape the dynamics of interactions within social insect colonies, worker activity rhythms might be an important factor affecting pathogen transmission and might even underlie certain aspects of organisational immunity. Although this hypothesis has received little attention so far, it is supported by one recent empirical study on social networks in the ant *Temnothorax albipennis* (T Richardson and T Gorochowski, unpublished). This study investigated the spread of agents with indirect transmission mode, such as pheromones or pathogens transferred via contaminated substrates, and showed that activity bursts at the colony level hinder agent propagation, because they introduce heterogeneities in the temporal sequence of interactions.

Modulation of social contacts

Spatial and temporal aspects of worker activity determine the likelihood of individuals meeting. Upon meeting, individuals can however decide whether or not to prolong their interaction and to initiate closer contact, such as grooming or trophallaxis. Because the duration and closeness of an interaction directly influence pathogen transmission risk, these decisions are expected to have a strong impact on disease spread, although the link between individual behaviour and colony-level disease dynamics remains to be investigated in more detail.

It has been suggested that honeybee workers might modulate social contacts depending on the age of interacting partners, thus reinforcing social segregation between age groups and providing prophylactic organisational immunity [38]. Electrophysiological recordings indeed showed that the antennae of old and middle-aged honeybee workers are more sensitive to stimulations with the odour of workers from their own age groups than with the odour of young bees, which could constitute the basis for age-dependent modulation of social contacts. Disentangling the respective roles of spatial segregation and individual decisions in generating age-based interaction biases will be crucial in determining the importance of behavioural modulation in mediating organisational immunity.

In ants and in the honeybee, pathogen exposure is known to trigger changes in interaction frequencies among workers, although it is still unclear whether these changes constitute the basis for induced organisational immunity. There have been multiple reports of either increases [44,45] or decreases [43,59••,70] in the frequency of trophallaxis involving pathogen-exposed or immune-stimulated workers (but see [71]). In honeybees, *Nosema*-infected workers both increase their food intake and decrease their willingness to share food with nestmates [70]. They may therefore turn into 'sinks' in the trophallaxis network of the colony, because they have higher incoming than outgoing food flow. It was hypothesised that this may help contain disease by decreasing pathogen transmission risk from infected to healthy workers. Moreover, grooming of treated workers has been consistently reported to increase following pathogen exposure or immune stimulation in ants, termites and honeybees [43,46,47•,59••,71–75] (but see [44]). Although grooming reduces the infection risk of pathogen-exposed individuals via mechanical removal of infectious particles from their body surface [72,75], sometimes combined with chemical disinfection [76], it also increases the risk of pathogen transmission to the

Mechanisms of organisational immunity in insect societies. The diagram identifies collective and individual properties influencing group-level disease spread and their mutual interdependence. Properties known to play a role in prophylactic, induced, or both prophylactic and induced organisational immunity are shown in blue, red, and purple, respectively. * see Box 1; ** see Table 1.

Table 1

Agent-based models and empirical studies of organisational immunity in social insects. For each study, the host species and (if relevant) the pathogen or non-pathogenic proxy considered are given, as well as the individual behaviour(s) studied, the size of experimental groups, and a mention of whether the authors formally investigated interaction patterns, whether they monitored the propagation of pathogens, non-pathogenic proxies, or information through the group, and whether experimental controls and/or theoretical null models were used. For studies involving pathogen-exposure or immune-stimulation of individuals, we provide the number of treated individuals first, followed by the number of non-treated individuals in each experimental group (e.g. '1 + 5 workers' means 1 treated worker put in contact with 5 untreated nestmates). [a]In these studies pairs of workers were inferred to be interacting if they were close to one another (spatial proximity); if they were close to one another and facing one another (spatial configuration); or if they were observed at the same location at the same or different times (spatial coincidence).

Study	Host	Pathogen or proxy	Behaviour studied	Group size	Interaction patterns investigated	Transmission monitored	Null model/control
Prophylactic organisational immunity in insect societies							
Interaction patterns and group-level transmission: cellular automata models							
Naug and Smith 2002 [15]	Model social insect	Ø	Contact	<300 workers	Interaction bias btw. 2 worker classes	Group-level spread modelled	Homogeneous null model
Pie *et al*., 2004 [50]	Model social insect	Ø	Contact	<1000 workers	Spatial heterogeneities	Group-level spread modelled	Null model
Fefferman *et al*., 2007 [29]	Model social insect	Ø	Contact; allogrooming	<1200 workers	Spatial heterogeneities	Group-level spread modelled	Null model
Interaction patterns and group-level transmission: empirical studies							
Naug and Smith 2007 [16]	Honeybee *Apis mellifera*	Microbeads	Trophallaxis	Observation hive (c. 4000 individuals)	Frequency and duration of trophallaxis	Group-level spread physically tracked	No
Naug 2008 [26]	Honeybee *Apis mellifera*	Ø	Trophallaxis	Observation hive (c. 1000 individuals)	Static network analysis	No	No
Feigenbaum and Naug 2010 [27]	Honeybee *Apis mellifera*	Radioactive food	Food transfer	Observation hive (c. 5000 individuals)	No	Group-level spread physically tracked	No
Scholl and Naug 2011 [38]	Honeybee *Apis mellifera*	Ø	Trophallaxis; antennal contacts	Observation hive (c. 1500 individuals)	Contact frequencies	No	No
Baracchi and Cini 2014 [39••]	Honeybee *Apis mellifera*	Ø	Spatial proximity[a]	Worker subset (n = 300) from observation hive (c. 4000 workers)	Static network analysis	No	No
Sendova-Franks *et al*., 2010 [28]	Ant *Temnothorax albipennis*	Food	Trophallaxis	Whole lab colony (42–95 individuals)	Static network analysis	Group-level spread inferred from trophallaxis duration	No
Blonder and Dornhaus 2011 [30••]	Ant *Temnothorax rugatulus*	Ø	Antennal contacts	Whole lab colony (6–90 individuals)	Static and dynamical network analysis	Group-level spread modelled	Null model for spread
Pinter-Wollman 2011 [31••]	Ant *Pogonomyrmex barbatus*	Ø	Spatial proximity[a]	Entrance chamber of whole lab colony (<131 workers)	Static network analysis	Group-level spread modelled	Null models for spread
Jeanson 2012 [53]	Ant *Odotonmachus hastatus*	Ø	Spatial proximity[a]	Worker subsets (n = 55–58) from field colony (c. 300 individuals)	Static network analysis	No	No

Mersch *et al*., 2013 [2••]	Ant *Camponotus fellah*	Ø	Spatial configuration[a]	Whole lab colony (122–192 individuals)	Static network analysis	Group-level spread modelled	No null model for spread, but see below
Quevillon *et al*., 2014 [32•]	Ant *Camponotus pennsylvanicus*	Ø	Trophallaxis	Standardised colony (1 queen + 75 workers)	Static and dynamical network analysis	Group-level spread modelled	No
Richardson and Gorochowski (unpublished)	Ant *Temnothorax albipennis*	Ø	Spatial coincidence[a]	Subset (queen + 14 workers) from lab colonies (47–134 workers)	Dynamical network analysis	Group-level spread modelled	Null models for spread
Heterogeneities in space use leading to spatial segregation							
Seeley 1982 [55]	Honeybee *Apis mellifera*	Ø	Spatial segregation	Worker subset (n = 100) from observation hive (c. 21,000 workers)	No	No	No
Naug 2008 [26]	Honeybee *Apis mellifera*	Ø	Spatial segregation	Observation hive (c. 1000 workers)	Static network analysis	No	No
Baracchi and Cini 2014 [39••]	Honeybee *Apis mellifera*	Ø	Spatial fidelity	Worker subset (n = 300) from observation hive (c. 4000 workers)	Static network analysis	No	No
Jandt and Dornhaus 2009 [56]	Bumblebee *Bombus impatiens*	Ø	Spatial fidelity	Whole lab colony (90–154 individuals)	No	No	No
Sendova-Franks and Franks 1995 [54]	Ant *Temnothorax unifasciatus*	Ø	Spatial fidelity	Whole lab colony (28–165 individuals)	No	No	No
Sendova-Franks *et al*., 2010 [28]	Ant *Temnothorax albipennis*	Food	Spatial segregation	Whole lab colony (42–95 individuals)	Static network analysis	Group-level spread inferred	No
Jeanson 2012 [53]	Ant *Odotonmachus hastatus*	Ø	Mobility	Worker subsets (n = 55–58) from field colony (c. 300 individuals)	Static network analysis	No	No
Mersch *et al*., 2013 [2••]	Ant *Camponotus fellah*	Ø	Spatial fidelity	Whole lab colony (122–192 individuals)	Static network analysis	Group-level spread modelled	Null model for spatial fidelity
Quevillon *et al*., 2014 [32•]	Ant *Camponotus pennsylvanicus*	Ø	Mobility	Standardised colony (1 queen + 75 workers)	Static and dynamical network analysis	Group-level spread modelled	No

Table 1 (*Continued*)

Study	Host	Pathogen or proxy	Behaviour studied	Group size	Interaction patterns investigated	Transmission monitored	Null model/control
Baracchi *et al*., 2010 [57]	Wasp *Polistes dominulus*	Ø	Spatial fidelity	Lab and field colonies (9–20 individuals)	No	No	No
High-pathogen risk tasks: specialisation and/or spatial isolation							
Arathi *et al*., 2000 [40]	Honeybee *Apis mellifera*	Freeze-killed brood	Hygienic behaviour	Observation hive (c. 3500 individuals)	No	No	No
Gordon and Mehdiabadi 1999 [63]	Ant *Pogonomyrmex barbatus*	Ø	Waste management	Whole lab colony (500–1500 individuals)	Yes	No	No
Hart and Ratnieks 2001 [35]	Ant *Atta cephalotes*	Ø	Waste management	Whole lab colony ($1–3 \times 10^4$ individuals)	No	No	No
Hart and Ratnieks 2002 [36]	Ant *Atta colombica*	Ø	Waste management	Whole field colony ($10^3–10^6$ individuals)	No	No	No
Recognition mechanisms and interaction heterogeneities							
Scholl and Naug 2011 [38]	Honeybee *Apis mellifera*	Ø	Responsiveness to age-specific CHC	Observation hive (c. 1500 workers)	Contact frequencies	No	No
Hart and Ratnieks 2001 [35]	Ant *Atta cephalotes*	Ø	Aggression towards waste workers	Whole lab colony ($1–3 \times 10^4$ individuals)	No	No	No
Induced organisational immunity in insect societies							
Interaction patterns and group-level transmission: empirical studies							
Otterstatter and Thomson 2007 [33]	Bumblebee *Bombus impatiens*	Protozoan *Crithidia bombi*	All contacts	Incipient colonies (1 queen + 4–6 workers)	Static network analysis	Group-level spread physically tracked	No
Modulation of interactions with pathogen-exposed individuals							
Richard *et al*., 2008 [46]	Honeybee *Apis mellifera*	Immune stimulation (LPS injection)	Locomotion; all contacts	1 + 10 workers	No	No	Sham handling; saline injection
Naug and Gibbs 2009 [70]	Honeybee *Apis mellifera*	Microsporidian *Nosema Ceranae*	Trophallaxis	2 workers	No	No	Sucrose control
Richard *et al*., 2012 [47•]	Honeybee *Apis mellifera*	Immune stimulation (injection of freeze-killed bacteria *Escherichia coli;* bead injection)	Locomotion; all contacts	1 + 10 workers	No	No	Sham handling; saline injection
Hughes *et al*., 2002 [72]	Ant *Acromyrmex echinatior*	Fungus *Metarhizium anisopliae*	Transmission; survival	1 worker; 1 + 2–5 workers	No	Transmission to nestmates	Triton X application
Aubert and Richard 2008 [43]	Ant *Formica polyctena*	Immune stimulation (LPS injection)	Locomotion; all contacts	1 + 10 workers	No	No	Sham handling; saline injection
de Souza *et al*., 2008 [44]	Ant *Camponotus fellah*	Immune stimulation (PGN injection)	Allogrooming; trophallaxis	2 workers; 1 + 1 workers	No	No	Ringer injection

Walker and Hughes 2009 [73]	Ant *Acromyrmex echinatior*	Fungus *Metarhizium anisopliae*	Allogrooming	4–6 + 21 workers	No	Transmission to nestmates	Triton X application
Bos *et al.*, 2011 [59••]	Ant *Camponotus aethiops*	Fungus *Metarhizium brunneum*	Allogrooming; trophallaxis	5 + 42–45 workers	No	No	Triton X application
Hamilton *et al.*, 2011 [45]	Ant *Camponotus pennsylvanicus*	Bacteria *Serratia marcescens;* immune stimulation (LPS injection)	Trophallaxis	2 workers; 1 + 1 workers	No	No	Ringer injection
Reber *et al.*, 2011 [74]	Ant *Formica selysi*	Fungus *Metarhizium anisopliae*	Allogrooming	11 workers; 1–2 + 3–28 workers	No	Transmission to nestmates	Tween-20 application
Konrad *et al.*, 2012 [71]	Ant *Lasius neglectus*	Fungus *Metarhizium anisopliae*	Allogrooming	1 + 5 workers	No	Transmission to nestmates	Triton X application
Rosengaus *et al.*, 1998 [75]	Termite *Zootermopsis angusticollis*	Fungus *Metarhizium anisopliae*	Allogrooming	1–25 workers; 5 + 10 workers	No	Transmission to nestmates	Tween-80 application
Spatial exclusion of pathogen-exposed or moribund individuals							
Rueppell *et al.*, 2010 [60]	Honeybee *Apis mellifera*	CO_2 exposure; hydroxyurea injection	Self-removal	Observation hive (c. 1500 individuals)	No	Group-level spread modelled	Null model
Baracchi *et al.*, 2012 [61•]	Honeybee *Apis mellifera*	Deformed wing virus	Enforced exclusion	Observation hive (c. 3000 individuals)	No	No	Healthy control
Ugelvig *et al.*, 2007 [48]	Ant *Lasius neglectus*	Fungus *Metarhizium anisopliae*	Self-removal	1 + 5 workers	No	No	Triton X application; UV-killed conidia
Heinze and Walter 2010 [58]	Ant *Temnothorax unifasciatus*	Fungus *Metarhizium anisopliae*; CO_2 exposure	Self-removal	20 workers; 10 + 10 workers	No	No	Natural death
Bos *et al.*, 2011 [59••]	Ant *Camponotus aethiops*	Fungus *Metarhizium brunneum*	Self-removal	5 + 42–45 workers	No	No	Triton X application
Rosengaus *et al.*, 1999 [62]	Termite *Zootermopsis angusticollis*	Fungus *Metarhizium anisopliae*	Alarm behaviour; escape behaviour	10 + 10 nymphs	No	No	No
Changes in tasks performed by pathogen-exposed individuals							
Wang and Moeller 1970 [64]	Honeybee *Apis mellifera*	Microsporidian *Nosema apis*	Foraging; guarding; queen care	Observation hive (c. 2500 individuals)	No	No	Healthy control

Table 1 (*Continued*)

Study	Host	Pathogen or proxy	Behaviour studied	Group size	Interaction patterns investigated	Transmission monitored	Null model/control
Woyciechowski and Moron 2009 [34]	Honeybee *Apis mellifera*	Microsporidian *Nosema apis*; CO_2 exposure	Foraging	Observation hive (size unknown)	No	No	Sham handling
Alaux *et al.*, 2012 [42•]	Honeybee *Apis mellifera*	Immune stimulation (LPS injection)	Queen care; foraging	Observation hive (size unknown)	No	No	Sham handling; ringer injection
Dussaubat *et al.*, 2013 [65••]	Honeybee *Apis mellifera*	Microsporidian *Nosema ceranae*	Foraging; flight activity	Observation hive (c. 4500 individuals)	No	No	Healthy control
Goblirsch *et al.*, 2013 [66•]	Honeybee *Apis mellifera*	Microsporidian *Nosema ceranae*	Foraging	Whole field colony (size unknown)	No	No	Sucrose control
Ugelvig *et al.*, 2007 [48]	Ant *Lasius neglectus*	Fungus *Metarhizium anisopliae*	Brood care	1 + 5 workers	No	No	Triton X application; UV-killed conidia
Bos *et al.*, 2011 [59••]	Ant *Camponotus aethiops*	Fungus *Metarhizium brunneum*	Brood care; nest defence	5 + 42–45 workers	No	No	Triton X application

grooming individuals [71,72]. The effects of increased grooming of infectious workers on colony-level epidemic size are still unknown, either because pathogen transmission was not monitored or because the groups studied involved too few individuals (Table 1). Colony-level pathogen spread could be either enhanced or hindered depending, for example, on the number, identity and degree of specialisation of the grooming workers, and these parameters should be considered in future studies. It should be noted that grooming workers usually show no or little increase in mortality [71,72,75], and that social contact with infectious workers can instead confer protection against later exposure to the same pathogen via social immunisation [45,48,71,77]. Transmission of low numbers of pathogenic propagules may therefore not be harmful to the host in certain host–pathogen systems [71]. It would be interesting to test whether colonies show more drastic changes in individual behaviour and collective organisation when exposed to more virulent pathogens.

Conclusions

Despite its recent formulation, the organisational immunity hypothesis has already stimulated many studies (Table 1). However, study effort has been taxonomically uneven, with disproportionately more work on bees and ants than on wasps and termites. In addition, group-level and individual-level approaches have not been equally applied in studies of prophylactic versus induced organisational immunity. On one hand, many studies investigated interaction networks in healthy colonies, revealing potential baseline pathways for transmission, although these have rarely been confirmed by the tracking of real, non-pathogenic proxies. On the other hand, behavioural changes induced by pathogen exposure have been mostly studied in small groups, and their effects on overall network structure and colony-level transmission dynamics are yet unclear. Studies investigating further the interplay between individual and collective processes, and confirming group-level dynamics by physically tracking real pathogens or non-pathogenic proxies, are therefore called for. A particularly interesting avenue for research would be to investigate how colony size might influence the manifestation and effectiveness of organisational immunity.

We believe that empirical studies of organisational immunity would also benefit from a tighter connection with theory. Epidemiology has generated many useful analytical tools and testable predictions that are usually not exploited to their full potential in empirical work. In addition, theory may help understand the idiosyncrasies of specific host–pathogen systems: different interaction networks underlie the spread of pathogens with different transmission modes, and this should influence both disease spread dynamics and the potential for the host to express organisational immunity. Combining empirical work with models fitted to specific host–pathogen systems is thus likely to be informative.

Understanding the effect of organisational immunity on epidemiology of insect societies poses both technical and theoretical challenges. First, studies on whole colonies have been rare, due to the technical difficulties of tracking a large number of individuals. However, automated approaches overcoming this constraint are becoming increasingly available (reviewed in [3••]). Second, choosing appropriate null models in theoretical studies can be challenging. Third, the empirical establishment of constitutive transmission pathways in healthy colonies requires the use of non-pathogenic proxies. Choosing an appropriate proxy, having similar transmission properties as real pathogens but inducing no behavioural changes in the host, is not trivial. Fourth, caution is required when interpreting pathogen-induced behavioural changes, since they can reflect pathogen manipulation or disease side-effects rather than host adaptation. Finally, it should be noted that pathogen transmission *per se* does not necessarily reflect disease spread, since transmission of low pathogen levels across the network can sometimes confer reduced susceptibility to disease by social immunisation [71]. This highlights the necessity to study the effects of pathogen transmission on the host in detail and to incorporate immunisation effects into epidemiological models.

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