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Social insect symbionts: evolution in homeostatic fortresses

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The massive environmentally buffered nests of some social insects can contain millions of individuals and a wide variety of parasites, commensals and mutualists. We suggest that the ways in which these homeostatic fortress environments affect the evolution of social insect symbionts are relevant for epidemiology, evolutionary biology and macroecology. We contend that specialized parasites will tend to become less virulent and mutualists less cooperative, compared to those associated with solitary or small-colony hosts. These processes are expected to contribute to the very high symbiont diversity observed in these nests. We hypothesize that biodiversity gradients in these hotspots might be less affected by abiotic latitudinal clines than gradients in neighboring 'control' habitats. We suggest several research lines to test these ideas.

Social insects and the homeostatic fortresses they create

An ant colony of any size is always an impressive sight, but one containing five million sisters certainly qualifies as one of the 'great achievements of organic evolution' [1]. Insect societies (ants, termites, some wasps and bees; Box 1) have developed multiple forms of division of labor, efficient ways of communication and spectacular feats of engineering in nest building and trail construction. The major milestones of insect social evolution and self-organized collective behavior have been intensively studied over recent decades [2], but the evolutionary consequences of insect societies altering their own environments have received less attention. This is surprising, because it is now 40 years since it was first noted that the interior of a large ant colony represents a radically different environment from that encountered beyond its borders, a concept encapsulated in the metaphor of a colony as a 'factory constructed inside a fortress' [3].

The nests that large insect societies create provide unique, environmentally buffered patches of habitat for many other organisms. The distinctiveness and quality of such patches are a direct function of the size and longevity of the colonies involved. Societies of ants and termites are remarkably long lived (Box 1). They can achieve this longevity by recruiting new queens at regular intervals, but also the queens (and kings in termites) themselves can have life spans of decades because the colony interior is a predator-free space where selection will tend to reduce rates of aging [4] (Box 1). Long life span of reproductives, large colony size and a homeostatic nest environment have thus evolved in concert because of positive mutual feedback [5]. Typical examples in the tropics are the 3 m high termite mounds in dry savannas that employ air-conditioning chimneys to maintain constant optimal conditions for fungus gardens, leaf-cutting ants that occupy subterranean living quarters comparable to the size of an average city apartment and nomadic bands of army ants constructing a living nest of worker bodies in temporary bivouacs (Figure 1). Temperate zone equivalents are thermoregulated honeybee hives and 2 m high nest mounds of boreal wood ants that maintain metabolically heated 'cellars' to survive −25°C winters (Figure 1).

The other organisms that have adapted to homeostatic life in insect societies can be collectively referred to as symbionts (symbiosis literally means 'living together'; Box 2). They are usually considerably smaller than their hosts and can be parasites, commensals, mutualists or a combination of these, depending on context [6,7]. In this essay, we offer several opinions about how long-lived, large, environmentally buffered colony environments can shape the ecology and evolution of symbionts in ways that are quite distinct from the forces acting upon symbionts of solitary and gregarious organisms that normally lack such homeostatic fortress environments. We do so by focusing on the interfaces of evolutionary biology, epidemiology and macroecology. We suggest that parasites of long-lived insect societies might generally be less damaging than those associated with nonsocial hosts, because homeostatic colony life will tend to reduce virulence. In the same vein, mutualists of advanced insect societies could fail to achieve maximal productivity. They are predominantly ectosymbionts [8], which implies that they are prone to attracting their own parasites and likely to maintain independent and sexual reproductive agendas that are costly for the host. We combine these arguments to infer that advanced insect societies are bound to create biodiversity hotspots that are interesting for comparative macroecological study, because they extend into dry and higher-latitude ecosystems that normally lack biodiversity hotspots.

Why parasites of long-lived insect societies are expected to be nonvirulent

Parasites, by definition, negatively affect hosts and this is termed virulence. Our understanding of virulence evol-

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Box 1. From an acorn to an oak

Social insect biology and social organization vary widely. Here we try to give a flavor of this incredible diversity and ask what it means for co-occurring symbionts.

Life history

Nests of social insects vary enormously. The diminutive ants of the genus *Temnothorax* can squeeze an entire colony of a few tens of individuals into an acorn and shift regularly as housing needs change, whereas the massive insect societies that are the focus of this paper have life histories reminiscent of large trees [23] and can occupy huge areas (Figure 1). Societies of ants and termites, and in some cases those of bees and wasps, are often remarkably long lived, an extreme case being that of a putative 800-year-old ant colony in the Amazon [57]. Like full-grown oaks, these mature societies are almost indestructible (see Box 3 for examples of human-mediated exceptions, leading to massive oak death and homeostatic colony collapse in honeybees). Many of them have specialized soldier castes and, in some termite species, the royal pair is actually ensconced within a concrete-hard chamber [58]. Such large insect society fortresses are predator-free environments where the queens (and kings or their stored sperm) can, in line with life-history theory for the evolution of senescence [59,60], live for several decades [4]. These extraordinary life spans have been able to evolve because the reproductive 'germline' of the colony (inseminated queen in Hymenoptera and queen/king pair in termites) is protected by thousands and sometimes millions of short-lived, disposable altruist workers, willing and capable to self-sacrifice when external threats occur.

Compartmentalized nest structure

The internal structure of insect society nests develops ontogenetically over a colony's lifetime. Just as 'mighty oaks from little acorns grow,' nests have simple stages at their foundation that can develop into large multicompartment complexes such as, for example, a 40 m wide weaver ant nest with half a million workers in a tropical canopy that was initiated by a single founding queen. The special homeostatic fortress conditions that we outline here as being important for the evolution of parasite virulence are only relevant when societies pass beyond a 'homeostasis threshold.' This transition will differ between taxa and might be something like 20 000 individuals for a species where colonies could eventually become 5 million, or 2000 individuals when colonies are destined to reach half a million. Field research to discover when colonies begin to resist external perturbations would be useful, both within and across species, whereas laboratory manipulations could address how numbers and adaptive compartmentalized architecture interact to minimize temperature and humidity fluctuations. Such focused studies into the occurrence and ontogeny of homeostatic fortresses could simultaneously address whether the presence of symbionts is state dependent, that is, whether parasites or mutualists can recognize that a potential host colony is above or below the threshold to qualify as a very safe environment. Ultimately, such data could address whether parasitic or mutualistic symbionts respond to such thresholds and whether their respective virulence or service is hard wired or plastic and condition dependent.

ution and epidemiology (Box 2) has been greatly informed by mathematical modeling. Although this body of theory has started to include populations that are structured by group living [9], we will argue that the unique factors inside homeostatic nest patches will require more complex models to explain the evolution of virulence in parasites of advanced insect societies [10]. To help inspire such efforts, we offer a series of verbal arguments.

First, the protective nature that a nest affords lowers extrinsic host mortality, with consequences for the evolution of virulence. In theoretical models where co-infection is absent, the level of extrinsic host mortality shapes virulence [11]. Simply put, grow fast if your host is likely to die early from some other cause, but exploit your host in a sustainable fashion if you can control its demise yourself. This implies that the same predator-free fortress environment that selects for long-lived social insect reproductives [4] might also select for reduced virulence.

The number of potential hosts has been predicted to increase virulence and, in particular, evolutionary biologists have usually considered very high densities of related individuals in colonies as a powder keg for explosive epidemics. However, this paradigm has recently been questioned [12], and it is also evident that the high levels of prophylactic disease defense that are typically seen in large insect societies are effective in preventing catastrophic outbreaks of disease [10,13,14] (Box 3). In fact, highly virulent parasites capable of wiping out whole colonies are unknown in large societies (with the exception of the domesticated honeybee; Box 3). When high worker numbers and coordinated hygienic defense prevent most infections from getting a foothold inside the fortress, this will likely impose selective pressure on parasites to reduce virulence. Efficient colony-level selection for host defenses might thus dampen, rather than escalate, host–parasite arms races and instead turn epidemic parasites into chronic symbionts that inflict only mild damage, leading to little selection for early detection and elimination of the parasites.

Virulence theory predicts higher virulence when genetically dissimilar parasites compete with each other inside the body of a single host [15,16]. In large societies, there can be hundreds of thousands or millions of individual workers and this will reduce the probability of single individuals picking up multiple infections. Therefore, high numbers of potential hosts could lead to reduced opportunities for parasite–parasite competition, leading to lower virulence.

Another important factor that affects the observed levels of virulence is the mode of transmission. Vertically transmitted parasites rely on host reproduction for transmission, and thus have lower virulence compared to horizontally transmitted parasites, which do not require reproducing hosts [17]. The relationship between horizontal transmission and higher virulence is supported by both theoretical and empirical findings [18,19]. In social insects, we contend that this relationship might not hold. Although examples of lethal horizontally transmitted parasites exist, these mostly concern parasite-induced behavioral changes in hosts that vector the parasites out of the colony to infect individuals of other colonies or different types of hosts [20]. When horizontal transmission is within the nest (worker-to-worker), it can be functionally equivalent to vertical transmission for the purposes of virulence models [10]. This is because a defining trait of social insects is that multiple offspring cohorts overlap, so that an adult worker passing on an infection to a larval sibling is functionally equivalent to a queen transmitting an infection to one of her eggs. This parallels a mixed vertical and horizontal transmission route in human tribes where horizontally transmitted microbes are more likely to be passed on to cohabiting kin than to strangers [21,22]. In both human and insect societies, the presence of multiple secure options for 'vertical' transmission is likely to trade off favorably

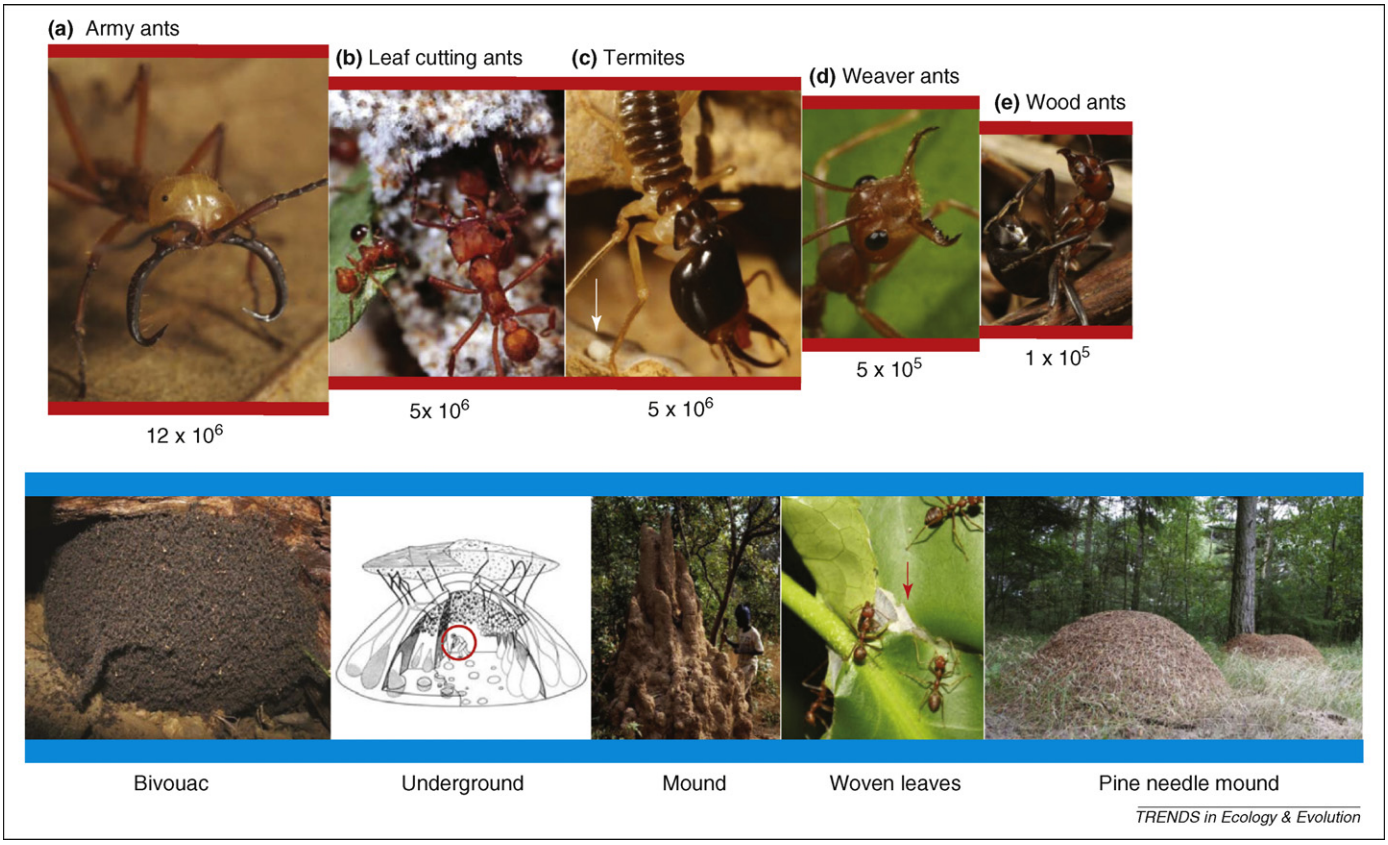

Figure 1. Representative taxa and nests from the large insect societies. For army ants **(a)** and termites **(c)**, individuals belonging to the solider caste are shown. Two different castes (major and minor) are evident on the fungus garden in the leaf-cutting ant example **(b)**. In the termite nest (c), the solider is traversing a fungal comb on which a fungal nodule can be seen (white arrow). For weaver ants **(d)** and wood ants **(e)**, typical defensive behavior is shown; the wood ant worker is spraying formic acid from the abdomen tip. Regarding the nest images, the bivouac of the army ants (a) consists of interlocked individuals. The leaf-cutting ant nest (b) is a drawing with a man (circled) to demonstrate scale; a man is also shown standing beside the termite nest (c). The leaf nests of weaver ants (d) are woven with silk (red arrow) produced by the larvae, and the wood ant nest (e) is within a conifer forest. Photo credits from top left: D. Kronauer, K. Lechner, D. Hughes, D. Hughes, D. Kronauer, D. Kronauer, D. Aanen, D. Hughes, D. Kronauer. The drawing is modified from J.C.M. Jonkman [6].

with the uncertain success of horizontal transmission between groups, so that many diseases might have been selected to become avirulent chronic infections rather than virulent epidemics.

The distinctive life histories of social insect hosts add further reasons for expecting low virulence of parasites (Box 1). It is worthwhile to note that large insect societies share five life-history traits with trees: large size, low mortality at maturity, high propagule mortality, modular growth and a sessile lifestyle [23]. Concepts from naturally coevolved plant pathogen systems can therefore be as relevant for understanding the evolutionary ecology of social insect symbionts as animal epidemiology models are. Although we know much less about diseases in naturally evolved systems such as tropical forests than about, for example, the fungi that infect economically important crops [24,25], overall the data suggest that most infections of mature tropical trees are not devastating but rather form a diverse community of benign chronic pathogens [24–26]. In particular, leaf diseases are renowned for their mild effects and it is indeed this category that is best comparable with diseases that affect the workers of massive insect colonies (Box 3). Tree defenses such as tolerance, leaf abscission and the ability to regrow or relocate resources away from disease [25,27,28] all have functional parallels in ants and termites, which accept high parasite loads, 'drop off' infected parts of a colony by walling in diseased areas or individuals, and relocate away from disease [10,29–31]. Tree leaves are short lived and disposable relative to stems [27], just like insect workers relative to queens [6], so that minor losses will hardly affect reproductive success. This implies that a virulent pathogen killing some workers belonging to a large homeostatic insect society is in fact nonvirulent from the perspective of the colony [10,32]. By contrast, plant diseases affecting seeds, saplings, flowers or trunks can be much more damaging for germline survival and fitness [25]. Such diseases often increase juvenile mortality or gamete mortality, similar to insect pathogens affecting mostly founding queens or incipient colonies.

To summarize, we expect that social insects with large colonies will have accumulated a much higher load of diverse, low-cost parasites over evolutionary time than comparable species with small colonies (Box 1) or solitary sister groups. We therefore would like to encourage focused comparative surveys to provide quantitative tests of this idea (Box 3).

Benign ectosymbiont diversity begets further diversity

The unique conditions inside large homeostatic fortresses that we have argued affect parasite virulence might also be important when considering mutualists. In particular, the stable environment of homeostatic fortresses facilitates the formation of complex communities where mutualists

Box 2. Expansion of some of the terms used

Here we provide some background to the key concepts used in this article, as well as some history of the development of the field.

Symbiosis

The term symbiosis was coined in 1879 by the plant pathologist Anton de Bary, who did pioneering work on fungal diseases of plants [61]. In its original formulation it means the permanent association between two or more specifically distinct organisms at least during part of their life cycle. Symbiosis therefore includes mutualisms (in which both parties benefit), commensalism (in which neither suffers) and parasitism (when one benefits at the expense of the other). The term symbiosis is often used synonymously with mutualism so that the negative aspects are excluded. Irrespective of the definition adopted, interactions between two species are best viewed as a continuum of costs and benefits with parasitism at one end and mutualism at the other. This implies that mutualisms are best considered as 'reciprocal exploitations' where both parties parasitize each other [62] while retaining a win-win balance.

Virulence

The term virulence is often used differently by invertebrate pathologists, plant pathologists, medical researchers and evolutionary biologists [63,64]. Evolutionary biologists typically consider virulence as the loss of host fitness due to parasites which ranges from outright death to reduced fecundity, lower mass and/or altered behavior [17]. Virulence is thus a product of the interaction between host and parasites [65] and could increase if hosts are stressed (context-dependent virulence). We currently have a far greater understanding of virulence from models than from empirical studies, although recent work on microbes is providing new opportunities for testing model predictions on the evolutionary dynamics of virulence (e.g. [66]).

Epidemiology

Epidemiology is the study of 'what is upon people' (Greek: *epi* = upon; *demos* = people; *logos* = study), but the term is used for animal and plant disease as well, particularly in mathematical models that seek to understand rates of parasite population increase. Such approaches, which have their foundation in Fisher's intrinsic rate of increase concept, were pioneered by Roy Anderson and Robert May in a series of papers from the late 1970 s (see references within Ref. [67]). Since then, the Anderson/May SIR models have become key instruments for understanding the dynamics of symbiosis in general and parasitism in particular.

Macroecology

Macroecology seeks to understand the factors and processes that govern the distribution of organisms, be they individuals, populations or species. Macroecology considers large spatial scales (regional, global) and long temporal scales (decadal, millennial) and relies upon large databases.

Box 3. Pestilence-stricken multitudes or panacea? The devil is in the details

There are two prevailing and mutually inclusive views of the role of parasites in colonies of social insects. The first considers a colony as an arena of disease with pestilence either running riot or trying to break into the fortress [10]. The other considers the colony as a tightly integrated factory where the slightest whiff of disease rings chemical alarm bells that prompt an array of cures such as antibiotics, hygienic behavior and live quarantine of infected individuals (reviewed by Ref. [14]). These cures are accompanied by an exhaustive prophylactic investment in disease monitoring. Real-life situations will likely be somewhere in between these two views, and be contingent upon which host and which parasite are considered (see Ref. [8] for a recent review). The devil is, as always, in the details, but tentative generalizations can be made. Small societies such as annual paper wasps and bumble bees or short-lived perennial *Temnothorax* ants are more likely to live with diseases that they try to outreproduce, whereas large perennial societies are only sustainable as long as they can prevent sweeping epidemic infections and keep chronic disease loads down. Likewise, it matters whether pathogens are microparasites (bacteria, viruses, some fungi) or macroparasites [8,10,67].

Much of what we know about social insect diseases is still based on studies of honeybee parasites. The honeybee builds large nests (50 000 individuals) that are thermally regulated and can thus be considered as homeostatic fortresses. Highly virulent diseases (*Varroa destructor*, CCD, Cape honeybee social parasitism) commonly destroy these fortresses, which seems to run counter to our argument of selection for reduced virulence. However, these parasites are all emergent infectious diseases which have encountered new hosts as a result of human trade and transport [68–70]. Our testable prediction therefore remains that mature homeostatic insect society fortresses do not normally succumb to epidemic parasites in their natural settings. Likewise, the tree analogy that we offer here (Box 1) is not invalidated by the highly virulent Sudden Oak Death that kills not only mature trees but whole forests, because these epidemics are also products of recent human activities [71,72].

The honeybee is an important model for advanced social evolution because it is the best-studied social insect and among the best-studied animals. Its genome has been sequenced entirely and offered the interesting finding of having significantly fewer immune genes than expected [73]. Further comparative genomic approaches will be needed to decide whether this is an artifact of domestication or evidence for colony-level behavioral defenses having made some of the individual immune genes obsolete. Recent metagenomics work has confirmed a high diversity of viral, bacterial and fungal endosymbionts [68], a result that also begs for additional comparable microbiomes to determine whether this result is peculiar to the honeybee or a general characteristic of advanced social insects.

can themselves be targets for parasites leading to a reduction in mutualist performance for the social insect host. Among the numerous mutualisms involving insect societies, the farming practices that independently arose in fungus-growing ants and termites are both relatively well studied and highly sophisticated [31,33,34]. These farming insect societies have been evolutionarily stable through tens of millions of years, most likely because they evolved mechanisms to protect their crops by optimal schedules of disease monitoring and quarantine [31,33]. Despite these effective defenses, diffuse coevolution can still be observed as the crop fungus is attacked by a specialized fungal pathogen and defended by domesticated actinomycete bacteria that the ants rear on their own bodies for antibiotic production [35,36]. These biocontrol mutualists are, in turn, themselves parasitized by a black yeast that compromises their efficacy [37]. Whether termite fungus garden mutualisms are equally complex remains to be seen, but it seems to be a safe assumption that additional symbionts could be found [38]. Similar scenarios where mutualists become less profitable owing to increasingly complex interactions that are facilitated by homeostatic fortress living likely apply to the numerous forms of animal husbandry that are practiced by ant societies when they tend aphids and caterpillars for sugar secretions [39]. These mutualistic interactions are also susceptible to performance-reducing developments, as the multiple transitions toward parasitism among lycaenid caterpillar–ant associations indicate [40] (see discussion in Ref. [41]).

With the data at hand, it seems clear that most insect society symbionts are ectosymbionts (living within the colony but not within the cells or tissues of individuals)

rather than endosymbionts [8,10]. Even the microbial gut communities of termites are formally ectosymbionts, as they tend to rely on horizontal transmission and are thus in regular contact with the environment. Mutualistic ectosymbionts of large societies might not be fully cooperative if they have retained their own agenda of independent reproduction, leading them to allocate resources into functions that are not in the interest of the host. The fungus garden mutualists of both termites and ants have in fact maintained traits that serve their selfish interests: ant fungi aggressively compete with genetically different nonresident strains [42] and termite fungi regularly produce sexual fruiting bodies that their hosts cannot eat [34]. Such traits are analogous to virulence (Box 2), as they reduce the benefits to the host. The maintenance of independent reproductive agendas in addition to reducing the performance of ectosymbionts for their social insect partners can thus also lead to a high diversity between colonies.

In summary, the unique conditions inside homeostatic fortresses could affect the payoff that mutualists provide to their social insect partners because the stable conditions can lead to mutualists becoming hosts to their own parasites, or cause mutualists to maintain their independent reproductive agendas. Thus, mutualists of homeostatic fortresses would provide interesting comparisons with mutualists of either nonsocial organisms or social insects with less advanced social systems.

Do insect society symbionts have shallow latitudinal biodiversity gradients?

We have suggested that the unique conditions in nests of large insect societies are expected to produce highly diverse communities of relatively avirulent pathogens and moderately benign mutualists. The modest information available indicates that symbiont diversity is indeed very high: at least 111 families of arthropods in 17 orders are known to be associated with ant colonies alone [6,7]. Even some commensals that do not interact directly with ants prefer colony life, as up to seven times as many earthworms can be found inside ant nests than in the surrounding soil [43]. Yet, this richness has hardly been systematically analyzed and we could thus have only seen the tips of these symbiont icebergs. Systematic surveys of microbial biodiversity are lacking (Box 3) and the traditional macrofauna biodiversity surveys using fogging, netting and transect walks will miss most of what lives inside colonies. Targeted sampling will thus be needed to access the full biodiversity of insect society nests underground, within hollow trees and in the canopy. Because social insects top the biomass index in most terrestrial biomes [44–46] and parasites themselves are recognized as having a high biomass in general [47,48], we can reasonably expect that social insect symbionts could contribute significantly to both ecosystem biodiversity and biomass.

Homeostatic fortresses can also foster high biodiversity in unusual places and could thus serve as useful test subjects in macroecological studies (Box 2). Latitudinal diversity gradients, with free-living species diversity being greatest in the humid tropics and decreasing toward higher latitudes, are a well-documented, highly robust and repeatable phenomenon [49,50]. The heat-preserving mounds of wood ants have allowed them to go above the Arctic Circle in their expansion out of glacial refugia [23], whereas the greenhouse nest-building technology of farming ants and termites have allowed them to export a tropical rain forest fungus to dry savanna and dessert biomes [31,51,52]. Comparative symbiont biodiversity surveys could therefore test whether homeostatic insect society fortresses differ from the classic latitudinal biodiversity gradient by showing shallower declines of symbiont diversity than their free-living sister clades in the immediate surroundings.

Perspectives

We have entered a new era in understanding the complexity and diversity of Darwin's tangled bank, with symbionts claiming an increasingly important position in biodiversity assessments [47,53–55]. Despite concerns about emerging diseases and possible pandemics (e.g. [56]), it has also become clear that many potentially virulent pathogens are fairly harmless as long as they are imbedded in a rich natural community of other symbionts associated with the same host [47]. Insect societies represent large-scale natural experiments in social organization that are much closer in scale and complexity to our own societies than the tribal bands of our closest great ape relatives. Focused interdisciplinary studies of the diverse symbiont communities of complex insect societies will not only offer crucial insights into the evolutionary stability of social life but also into the ecological opportunities that homeostatic fortress living provides.

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