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INVITED REVIEW

Intersection between parental investment, transgenerational immunity, and termite sociality in the face of disease: a theoretical approach

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Abstract

We developed a novel, resource-driven theory for transgenerational immune priming (TGIP). From this theory, two models were constructed, one termite-specific and the second one, applicable to other social species as well to elucidate whether TGIP should be expressed and whether colony ontogeny and demography influence parental immunological contributions, their magnitude and their duration. Both the nuanced (detail-rich) and simplified (yet generalizable) models may ultimately shed light into whether TGIP is equally adaptive across different stages of colony maturation and if the mechanisms underlying TGIP are fixed or if these mechanisms exhibit a certain degree of plasticity depending on pathogenic risk and/or age of the colony and its accompanying demographic composition. Furthermore, our models can help answer if the immunological nature of TGIP can change from being a generalized immune response to perhaps a more highly pathogen-specific protection as the colony ages and as the risks of infection diminish. These models can also help elucidate whether the immune protection by parents toward progeny should result from contributions of prefabricated functional immune proteins, the transfer of immune elicitors from parents to offspring or whether TGIP should be based instead on epigenetic markers altering gene expression in the progeny. Through this synthetic empirically based approach, we hope to prompt novel testable questions that can ultimately provide a better understanding of the expression of TGIP, its magnitude and duration across generations including its adaptive value during the ontogeny of other eusocial insect species as well as other group-living non-eusocial species.

Significance statement

Transgenerational immune priming (TGIP), wherein parents transfer immune function to their progeny based upon their own pathogenic experience, has been broadly reported across the animal kingdom and yet, the specific mechanisms underlying TGIP and the evolutionary forces driving TGIP remain poorly understood. This is particularly true for eusocial insects where the complex nature of social interactions likely influence both the costs and benefits of TGIP. Here we provide a synthetic review of the TGIP literature and then use elements and concepts from the review to develop a dynamic state variable model for adaptive TGIP in termites in particular and insects with various degrees of sociality, in general. Key concepts to the model include colony-wide immunocompetence, resource wealth, and progeny quality/quantity tradeoffs. We use the models to make a number of novel predictions for adaptive TGIP in nature.

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Introduction

Parental investment theory postulates that adults who accurately perceive their surroundings and anticipate the needs of future offspring should be selected to manipulate and allocate resources to their progeny in a context-dependent fashion (Trivers 1972; Maynard Smith 1977; reviewed by Wade and Shuster 2002). In this way, the physiological needs of the offspring should match most environmental pressures and conditions (Sorci and Clobert 1995; Wade and Shuster 2002; Poulin and Thomas 2008; Storm and Lima 2010), increasing the survival of progeny and consequently, the lifetime fitness of the parent. When parents face pathogenic pressures, the transgenerational effects may be triggered by a variety of pathogenic microbes and immune-elicitors. Such pathogenic-induced effects across generations have been reported in solitary invertebrates and eusocial insects (Moret and Schmid-Hempel 2001; Little et al. 2003; Saad et al. 2005; Moret 2006; Sadd and Schmid-Hempel 2007, 2009a,b; Freitak et al 2009; Roth et al. 2010, 2018; Tidbury et al. 2010); yet the specific mechanisms underlying this phenomenon are not clearly understood (Grindstaff et al. 2003, 2006; Freitak et al. 2014; Salmela et al. 2015; Cole et al. 2020a). A detailed understanding of the environmental, biological and societal constraints and dynamics of parental resource provisioning, together with the corresponding fitness effects on offspring is therefore needed. Here, we generated a theoretical framework of conditional parental investment of eusocial insects that includes the parent's pathogenic history as well as the possible trade-offs among reproduction, parental immune defenses, the allocation of resources toward colony demography and resource allocation to future fertile progeny (Sorci and Clobert 1995; Storm and Lima 2010). The generation of this framework can serve as a stepping-stone for future empirical studies on whether parents transfer, in a heritable and conditional fashion, immune function to their progeny via transgenerational immune priming (TGIP).

TGIP has been reported across diverse taxonomic groups (reviewed by Roth et al. 2018; Tetreau et al. 2019; Mondotte et al. 2020) and researchers have identified the conditions and requirements that likely favored its evolution. For TGIP to be adaptive and for it to persist across both micro and macro-evolutionary time, a parent's exposure to a particular pathogen should provide a reliable cue that the environment poses pathogenic risks and that both parents and their offspring are likely to encounter the same pathogen in the future. This is conceivable when:

a) Pathogens are globally common but locally unpredictable and yet linger long enough in the environment for both generations to encounter them;
b) The hosts' generation time is relatively short (such that there is a great likelihood that the pathogen will persist across host generations);
c) Philopatry of both parents and offspring is high (low dispersal for parent and their offspring favors everyone encountering or re-encountering the same pathogenic stressors);
d) Hosts are long-lived relative to their pathogens (although no real consensus has been reached as to the role of longevity on immunocompetence (Miller et al. 2007; Fabian et al. 2018), and
e) The costs of generating immune responses are significant, thus selecting for the deployment of immune function across generations only when necessary.

Eusocial insects in particular, meet these conditions. The very definition of eusociality requires the overlap of generations within the same nest, which is colonized, at least during certain stages of colony development, by potentially heavy loads of diverse pathogenic microorganisms (reviewed by Schmid-Hempel 1998 and references therein). Given their nesting, feeding and foraging ecologies, prolonged individual- and colony longevity (Thorne et al. 2002; Kramer and Schaible 2013) and their social nature, eusocial insects are prime candidates to exhibit TGIP. Yet, only a handful of studies have addressed this phenomenon. Phenotypic and/or molecular evidence for TGIP in eusocial insects has been reported in the honeybees (Lopez et al. 2014; Salmela et al. 2015), bumblebees (Sadd et al. 2005; Sadd and Schmid-Hempel 2007; Barribeau et al. 2016), ants (Bordoni et al. 2018; Fuch et al. 2018) and recently, in termites (Cole et al. 2020a).

Pathogenic pressures across all eusocial insects, however, are not equivalent. Eusocial species nesting and/or foraging in soil and/or nesting in and feeding on decayed wood are likely under higher pathogenic pressures than arboreal or mound building species (Hölldobler and Engel-Siegel 1984; Rosengaus et al. 2003; Boomsma et al. 2005; Tunaz and Stanley 2009). Moreover, pathogenic exposure risks, their negative effects, the outcomes between competing physiological trade-offs (e.g., immunity vs. reproduction; Schwenke et al. 2016) and different types of TGIP are not necessarily fixed throughout colony ontogeny. Given these complexities, a theory of termite TGIP and perhaps other eusocial insects seems necessary to guide future research into this evolutionary significant and widespread phenomenon.

This work represents a synthetic review with two main goals. First, we review the pathobiology of termites through the lens of both life history and parental investment theories.

Second, we address the question: If we are to develop a TGIP theory, what should it look like? This is not a trivial question since such theories could take many different forms depending on which variables are included and the aims of such theories, possibly leading to many different interpretations of the TGIP phenomenon. Below we argue that, contrary to most previous static theoretical approaches, a dynamic theory is necessary to capture the changing social structure of a eusocial insect's colony and as such, better inform us about the realistic costs and benefits associated with TGIP. This necessary first step should then lead to explicit predictions and experimental tests of such. We zoom-in at the intersection of three important life-history attributes of eusocial insects while under pathogenic risk: parental investment, immune defenses and colony ontogeny (and its subsumed social structure such as caste and age composition) to generate new TGIP expression theory. This theory builds on the fact that the fitness consequences of these life-history attributes are at the nexus of colony success generating a complex and dynamic "fitness landscape." A conceptual version of our theory is shown in Fig. 1, which includes four different ecological scenarios under varying degrees of both pathogenic risk and trade-offs among life history traits. Further, we develop two analytical versions of this TGIP-expression theory, one that is detail-rich and the other, a more simplified version of the original. The former model is termite-specific while the latter is more general and thus, more applicable to organisms spanning the sociality spectrum (Fig. 1). Bear in mind that at this point, we are not performing formal analyses of our models. To do so would entail developing computer algorithms that emulate the mathematics described below (e.g., Roitberg and Mangel 2010), a separate project beyond the scope of this work on which we will report in the future. Instead, the focus of this current work is to introduce, as a first step, a novel approach to the question: when and under what conditions, in a eusocial insect colony, should TGIP be expressed? And, if TGIP is expressed, what is its nature, its magnitude and its duration? This is feasible by first laying down a theoretical resource-driven framework that incorporates explicit demographic structure, allowing for interactions among different variables.

Our detail-rich (i.e., nuanced termite model) conveys the dynamic interactions among three key life-history traits and their context-dependent consequences which in turn, influence the magnitude of the adaptive TGIP region (the intersection area in Fig. 1). Figure 1 reinforces the recognition that nature is complex. Thus, our model provides a realistic perspective on when to expect the expression of adaptive TGIP and its magnitude based on pathogenic loads and the dynamic (and potentially conflicting) life-history traits

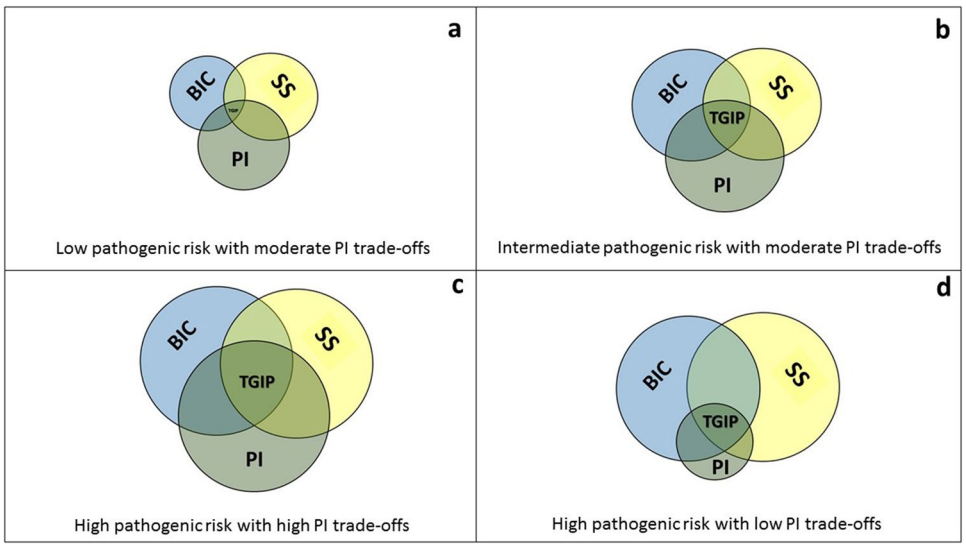

Fig. 1 Visualization of the current model through a Venn diagram. This composite indicates the contextual relative investments that the royal pair in termites (or perhaps only queens in the social Hymenoptera) devote towards Transgenerational Immune Priming (TGIP) given their local assessment of pathogenic risks (low, intermediate and high) and finite resource pool availability. The circles represent three important life-history traits in eusocial insects: Parental investment (PI), Baseline immune-competence (BIC) and the colony's social structure (SS) which is dictated by both colony ontogeny and demographic composition. The size of each circle represents the magnitude of the marginal returns (i.e., added benefits) from expression of TGIP. In this model, both resource availability and the amount of parental energy available to allocate to each of the three life-history traits is fixed and thus, the three life history traits are prone to experience trade-offs. The circles expand or contract depending on the contextual milieu surrounding a colony, and therefore, the magnitude of the adaptive TGIP region (intersection) is also affected. For additional details on this figure, see main text. Except for environmental pathogenic load and the concomitant investment allotted by parents towards baseline immune-competence, all aspects across all four scenarios (Fig. 1a, b, c, d) remain constant. Each panel of Fig. 1 is also influenced by the dynamics depicted in Fig. 2

(i.e., the expanding or shrinking circles in Fig. 1). TGIP models in the past have not necessarily included context-dependent variables. We envision three life history traits by which social insect offspring mitigate risk from pathogens: (i) Baseline Immunity (BIC) – defined as the physiological ability to prevent pathogenic infection, (ii) social structure (SS)—defined as demographic characteristics of a colony (age and caste distributions: eggs, different instar larvae, workers, soldiers, reproductives) that facilitate disease resistance via social interactions among nestmates, and (iii) parental investment (PI)—defined as the overall amount of resources that parents contribute to their progeny which ultimately, improve offspring quality in terms of enhanced protection against infection. The activation of each of these traits has an inherent energetic cost. Enhancing any one of them necessarily draws energy away from the overall resource pool that would otherwise fuel all three life-history traits. For example, enhancing quality of eggs via increased deposition of proteins (i.e., vitellogenins) is normally associated with a cost to the parents in the form of reduced fecundity (the classic quality-quantity tradeoff—Stearns 1992). Based on Fig. 1, we can seek the conditions that favor *TGIP as an alternative to further investment in any of the three life histories (BIC, SS, PI)* within an ecological context. Each of the Venn circles represents the *marginal gains from expressing TGIP* in the context of these life history traits. For example (Fig. 1c), when pathogenic risk is high and tradeoffs for investing in any or all three of the key life history traits are also high (when investment in one life history trait pulls away resources from the common pool of resources), TGIP would be widely favored. By contrast (Fig. 1a), when pathogenic risk is low and when tradeoffs from further investing in the key life history traits are also low, TGIP would rarely be favored. Another interpretation of Fig. 1a is that, given the low pathogenic risk context, offspring should perform well without further investment in any of the life history traits or in TGIP (hence the tiny TGIP region in the intersection of Fig. 1a). In Fig. 1b, the marginal gain circles are larger than in Fig. 1a because of increased gain from offsetting the greater risk from infection. Figure 1d further illustrates the importance of pathogenic risk. Notice that the space favoring TGIP in Fig. 1b and d is nearly identical despite differences in life history trade-offs. In Fig. 1d, the low PI tradeoff is, as above, again offset by even greater infection risk.

Notably, each panel represents the dynamics among life-history traits in the face of varying disease pressures during a fixed stage in the colony's development. In nature, however, each of these scenarios is concurrently influenced by available wood resources and the degree of colony maturation (i.e.,

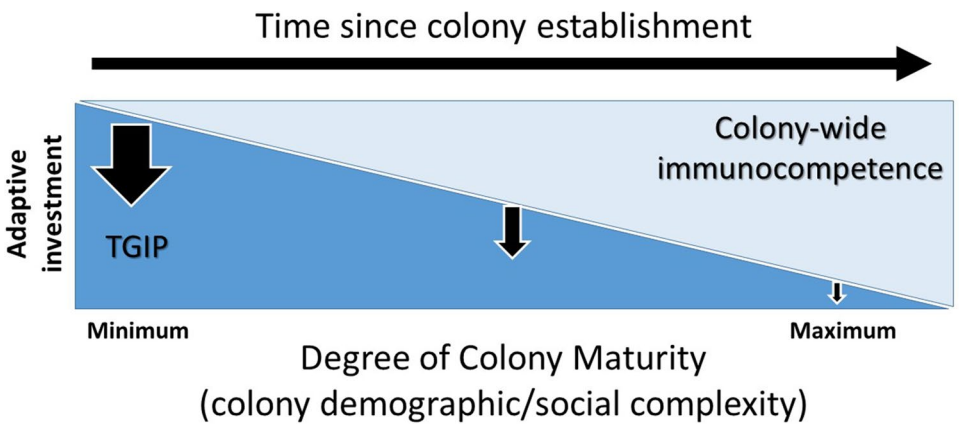

Fig. 2 Predicted adaptive investment toward Transgenerational Immune Priming (TGIP) and termite colony-wide immunocompetence as a function of colony maturation (x axis) and assumed relative risks of disease (arrow thickness) throughout the continuum of colony maturation. In the case of termites, colony-wide immunocompetence results as an outcome of social structure which in turn fosters emergent communal immune responses given the termites' eusocial lifestyle. However, when referring to our second more generalized model applicable to non-eusocial, yet group-living taxonomic groups, then the concept of "colony-wide immunocompetence" in Fig. 2 may be replaced by "communal immunity." Here, we use colony-wide immunocompetence as the emergent property of a colony whereby the combined individual- and colony-level mechanisms result in improved disease resistance of the entire interacting insect assemblage. We are assuming that TGIP and colony-wide immunocompetence are independent and have an additive effect on disease resistance. We anticipate the benefits accrued from TGIP should be significantly higher early during colony life as incipient colonies are under more stringent pathogenic pressures (larger black arrow) while concurrently lacking the social milieu that ultimately results in social/communal immunocompetence. The intermediate stage of colony maturation is likely under less stringent pathogenic pressures (medium black arrow) than the incipient stage thanks in large part, to the communal hygienic behavior of the more numerous within-colony population. The mature colony stage is even less prone to pathogenic pressures (small black arrow). We propose that once a colony surpasses the intermediate stage of colony development, the benefits of colony-wide immunocompetence (due to the presence of different castes and age distributions in the nest) offset the benefits of TGIP, as TGIP is likely to be more energetically costly to express than social means of disease control. This diagram should be interpreted in conjunction with Fig. 1

time elapsed since the inception of a colony). Thus, each panel of Fig. 1 is also influenced by the dynamics depicted in Fig. 2 where we provide a longitudinal view of TGIP value.

Here, the value of TGIP declines as an inverse of the magnitude of colony-wide immunocompetence which, based on empirical data, is assumed to increase with colony age and because it is unlikely that new pathogens enter the nest after founding in the log. In termites, the probability of successfully establishing a new colony by the monogamous reproductive pair is slim; under laboratory conditions and depending on the species, between 25 and 60% of experimentally naive founding pairs die within the first 20–30 days after pairing (Rosengaus and Traniello 1993a; Hartke and Rosengaus 2013; Cole et al. 2018; Cole and Rosengaus 2019). Although the cause of mortality in these studies was unknown, the majority of these deaths appear to be pathogen-related (either bacterial or fungal infections; RBR personal observations). Yet, in a longitudinal study, Cole and Rosengaus (2019) reported that the mortality of those remaining surviving colonies leveled-off after days 20–30 post-pairing, once the founding pair crossed the oviposition "checkpoint" and reached the initial growth phase. Hence, based on all this circumstantial evidence, we are confident that pathogenic pressures are particularly stringent early during colony foundation and that as colonies grow, they are better buffered against the negative effects of pathogens, likely due to communal adaptations to resist disease, including behavioral (allogrooming), biochemical (deposition of excreted antimicrobial glandular compounds), and individual- and societal-level immunological processes (i.e., variolation, sharing of immune function via social interactions; reviewed by Rosengaus et al. 2011a; see Section AIId below). We can thus imagine that the marginal returns from further enhancing TGIP will decline with colony age (Fig. 2). We recognize that the size of the lower triangle can vary as a function of host species and its particular ecological context. We captured the impact that colony maturation has on TGIP and the levels of investment in colony-wide immunocompetence in our formal models below (eq. # 1, 2, 4).

In what follows, we explicate our conceptual model presented in Figs. 1 and 2 and, in particular, we do so for one-piece nesting termites, such as the dampwood termite *Zootermopsis angusticollis*. There are good reasons for choosing this focal group. First, one-piece nesting termites are considered basal social insects (evolved ~ 150 million years ago; Chouvenc et al. 2021). The generation of these theoretical models using "basal" attributes can be particularly fruitful as it may provide insights into the factors promoting the origins and maintenance of TGIP in eusocial insects per se. Second, there is ample information regarding basal termite pathobiology in both young (early development) and mature colonies (Rosengaus et al. 2011a and references therein; Cole et al. 2018, 2020a, 2020b; Cole and Rosengaus 2019). Third, we have identified many of the costs and benefits of sociality as they relate to the generation of immune responses against both fungal and bacterial infections (Rosengaus and Traniello 2001; Calleri et al. 2006; Cole et al. 2018). Fourth, our research demonstrates that termites exhibit multi-level adaptations usually deployed simultaneously or sequentially to resist disease, including behavioral, biochemical, individual (both cellular and humoral responses) and societal-level immunological mechanisms (reviewed in Rosengaus et al. 2011a; Mirabito and Rosengaus 2016) as well as the significant role that the termites' mutualistic gut microbiome may play in the resistance against disease (Rosengaus et al. 2014). Fifth, we have molecular evidence for TGIP in *Zootermopsis angusticollis*: queens exposed to sub-lethal dosages of the Gram-negative bacterium *Serratia marcescens* prior to mating oviposited eggs with more than double the number of RELISH (an immune-related gene) transcripts (Cole et al. 2020a). The recent discovery that antifungal properties in embryos of *Z. angusticollis* exist as soon as embryos are oviposited (although their level of fungistasis increases during their ontogeny, Cole et al. 2020b), further support the notion that this most immature developmental stage has the immunological machinery to cope with pathogens. Parents, based on their immunological status, could conceivably manipulate such machinery to confer further protection to the next generation either by imbuing their eggs with pre-fabricated functional immune-related effectors, immune-elicitors or epigenetic information during oogenesis (Cole et al. 2020a). Any of these mechanisms could tailor immune-related parental contributions to offspring in a context-dependent fashion, ensuring that oviposited fertilized eggs (embryos) and future hatched instars/castes benefit from the transfer of information across generations. Finally, as noted by their name, one-piece termites draw upon a finite amount of wood resources (Abe 1987); this simplifies our models in that we need not consider outside-the-nest foraging effort as part of the TGIP strategy.

Given that termites exhibit many of the supposed attributes that are conducive to the expression of TGIP, we have built our theoretical framework based on known facts about termite pathobiology. Yet, our models can be easily modified to develop predictions for other soil dwelling eusocial insects such as ants, or sub-social species such as wood roaches or burying beetles, and more broadly to other organisms spanning the sociality spectrum. Given the putative cost of TGIP, we expect that many organisms, eusocial, subsocial and otherwise, will be forced to trade-off investment in immunity against other functions and such trade-offs will be highly resource-dependent; our theory makes explicit use of this resource-based trade-off.

Before describing the components of our models, we first provide background information on the different modalities by which TGIP can be attained and then, we integrate some of the

termite-specific ecological and physiological constraints with life-history theory by summarizing relevant natural history of *Zootermopsis*.

Background information

Mechanisms of TGIP

TGIP can be achieved through several mechanisms. First, after becoming infected and generating an immune response, queens can transfer (during oogenesis) pre-fabricated functional immune proteins (Fraune et al. 2014; Cole et al. 2020b), or immune-related transcripts (Seppola et al. 2009) or immune-elicitors such as bacterial (i.e., lipopolissacharides, peptidoglycans) or fungal (β, 1–3 glucans) byproducts (Salmela et al. 2015). The egg may also be permeable to the pathogen itself, which in turn, triggers the egg's immune responses (Freitak et al. 2014; Knorr et al. 2015; Cole et al 2020b). Finally, the pathogenic stress experienced by the queens could result in epigenetic markers added to the egg's DNA, thus modifying the egg's gene expression (Cole et al., 2020a). Any of these mechanisms or any combinations of these mechanisms could ultimately render progeny less susceptible to disease (Roth et al 2018; Tetreau et al 2019; Cole et al 2020a,b). Conceivably, paternal TGIP effects by the termite king could take place during copulation via sperm transfer and seminal fluids and/or accessory gland secretions. Clearly, additional empirical experiments are needed to elucidate which of these mechanisms plays a role in termite TGIP.

Zootermopsis natural history

Before delving into the nuanced model, we introduce some of the basic, unique and interesting aspects of *Zootermopsis*. Given that this basal termite genus has been the focus of much pathobiological and immunological research, it provided the biological backdrop against which the expression of termite TGIP occurs. Therefore, termite biology informed and anchored our nuanced model. Although differences on the basic biology described below exist across termite species, it is reasonable to consider the biology of *Zootermopsis* to be representative of most lower termites. All lower termites harbor both prokaryotic and eukaryotic unicellular mutualists in their hindgut, which in *Z. angusticollis*, have been implicated not only in the nutritional wellbeing of their host (Nalepa 1994) but also in influencing the termite's reproduction (Rosengaus et al. 2011b) and their ability to fight fungal disease (Rosengaus et al. 2014). This species lives in the Nearctic temperate forests of western North America (Eggleton 2000) and feeds on dead moist decayed/fallen wood (hence their categorization as dampwood termites). Given they do not forage for food outside their nest, but instead feed on the wood that also serves as their nest, *Zootermopsis* is considered a "one-piece nester" (Abe 1987). As such, it is reasonable to assume that, as colony size increases, *Z. angusticollis* will experience higher resource limitations than those other termite species in which feeding and nesting sites are decoupled (known as "multiple-piece nesters," Abe 1987). The combined effects of finite amounts of wood and low nutritional value of decayed wood (Shellman-Reeve 1990, 1994), set the stage for the termite's energy availability being both limited and limiting, promoting trade-offs amongst different life history traits (see Extrinsic State (a), below). The amount and quality of decayed wood will set limits to colony growth and its accompanying demographic composition and these constraints may explain why *Zootermopsis* colonies are relatively small, comprising only thousands as opposed to hundreds of thousands or millions of individuals (Thorne 1997). This species lacks sterile workers; immature individuals retain the potential for acquiring reproductive status whenever the original founders die (Thorne 1997). The potential trade-offs driven by the limited availability of resources (and thus, energetic currency) may be exacerbated by the fact that partially buried decayed wood is colonized by a variety of microbial organisms, many of which are pathogenic (see Rosengaus et al. 2011a and references therein). Under pathogenic risk, it is reasonable to assume that the relatively long-lived *Zootermopsis* parents (queen and king, Thorne et al. 2002) are forced to divert energy away from reproduction while coping with imminent infection, hence resulting in trade-offs between reproduction and immune-function (Calleri et al. 2006; Cole et al. 2018; Cole and Rosengaus 2019). Contrary to eusocial Hymenopteran species, *Zootermopsis* colonies (and most other termite species) establish new colonies by having queens and kings join in a monogamous mating system following their swarming flights (Fig. 3). These reproductives initially build a chamber within the decayed wood (copularium) where they mate and where on average (and under lab conditions), initiate oviposition ~ 16 days after pairing (Cole et al. 2018). If the new colony does not fail during the initial critical stages of colony foundation, the reproductive pair can survive an average of 4.5 years (Thorne et al. 2002). As hemimetabolous insects, first and second instar hatchlings are fully dependent on their parents (see Cole et al. 2018; Cole and Rosengaus 2019 for additional detailed information regarding the dynamics of reproductive output of incipient colonies). By the third instar, however, the larvae are contributing to colony labor to the same degree as any other older instar (Rosengaus and Traniello 1993b). Once a colony enters its ergonomic stage

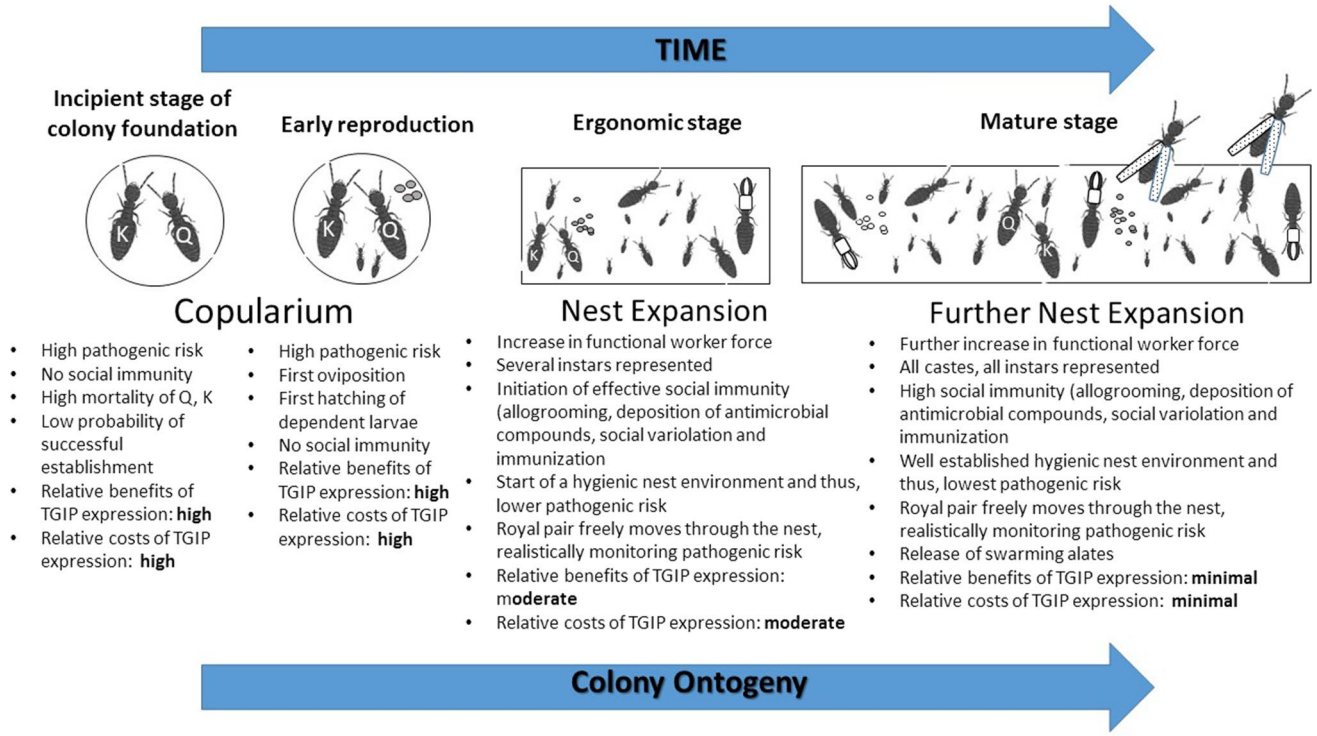

Fig. 3 Colony ontogeny of *Zootermopsis* from the time of colony foundation to maturation. Termites labeled K and Q represent the king and queen of the colony. Small ovals represent eggs. Termites of different sizes represent larvae of different instars. Termites with long sickled mandibles represent soldiers and termites with wings represent the next generation of winged individuals, which swarm away from the parental nest to seek a mating partner to establish an incipient colony. The timing to produce the new generation of alate dispersers is variable and can take place between 1.8 and 6.5 years after the original parents paired (Thorne et al. 2002). The bulleted information matches the expected pathogenic risks (based on empirical data) depending on the social structure of the colony throughout its life cycle. As the colony ages, its density increases, and both caste and age-composition of the worker force changes. This in turn, reduces wood resources, increases nest hygiene and lowers pathogenic risk. Given that the royal pair freely moves through the nest during the ergonomic and mature stages, it can realistically monitor pathogenic risk and thus, remain informed about whether investment in Transgenerational Immune Priming (TGIP) should occur as the colony matures. Expected relative benefits and costs of TGIP across the different life stages of a termite colony are also included

(Cole et al. 2018; Cole and Rosengaus 2019), it is composed of the reproductive caste (either the original royal pair or their offspring who can take over reproductive tasks in their absence), a multi-age larvae population (instars 1 to 6; with instars 1 and 2 fully dependent on parents and older nestmates and instars 3–6 serving as the functional worker caste), nymphs (also functioning as workers) and soldiers specializing in defense (Fig. 3; Rosengaus and Traniello 1993b; Thorne 1997). In contrast to other termite species where the queen and king remain sequestered in the royal chamber while tended by their workers, *Zootermopsis* queens and kings move freely throughout the galleries of the fallen wood nest (RBR personal observation). Their workers interact with the reproductive pair wherever queens and kings are found within the nest. Hence, the potential for the reproductives to "monitor" colony state and pathogenic risk within the nest is high, which likely influences their "decision" of whether to invest in TGIP or not. The queen seems to lay her fertilized eggs throughout the colony and her workers are responsible for piling them at multiple sites within the nest (RBR, personal observation). Other more specific details on the biology of this genus are presented alongside the description of our models and the resulting equations to couple and reinforce the significance of such specific traits in this theoretical exercise.

Bridging biology and theory: life history, constraints, and trade-offs may influence when and what kinds of TGIP are expressed

Immune responses, including TGIP, are energetically expensive. As such, their deployment incurs significant costs to the individual host and/or its progeny (Schmid-Hempel 2003; Trauer and Hilker 2013; Contreras-Garduño et al. 2014; reviewed by Tetreau et al. 2019 and references therein). As such, immunity, an important life-history trait that helps

offset imminent pathogenic stress, is often prioritized at the expense of other physiological systems, resulting in trade-offs, including those between immunity and reproduction (reviewed in Rolff and Reynolds 2009; Schwenke et al. 2016). Just like the generation of their own individual immune responses), TGIP is likely costly to the parents as well. Assuming there is no constraint in the evolution of TGIP, and given such costs, parents should express TGIP only when necessary (Fig. 1). For example, if pathogenic stress is infrequent in time and space, then, based on life-history theory, we anticipate those hosts not to exhibit TGIP (Garnier et al. 2012). On the other side of the spectrum, if pathogenic loads are diverse, consistently virulent and predictable in time/space, then natural selection would have promoted constitutive (always "ON"; as defined by Boots and Best 2018) levels of TGIP. A third intermediate alternative is possible: if pathogenic stressors are inconsistent in time/space but still pose significant pressures on the infected host whenever present, then, parents should invest in TGIP in a context-dependent fashion, engaging in TGIP *only* when conditions necessitate it (Pigeault et al. 2016). In other words, TGIP should exhibit a certain degree of plasticity. In this way, parents can balance the negative energetic costs associated with the transfer of immune function across generations and the need for maximizing their own reproductive success (Fig. 1). When focusing on eusocial insects, the maximization of reproductive success by queens and kings is measured not by the number of overall progeny produced (as workers and soldiers are sterile), but rather by the number and quality of future reproductives that the parental colony produces [i.e., number of dispersing winged (alates) individuals with reproductive potential; Fig. 3; Oster and Wilson 1979)]. For convenience sake, we disregard the timing of when the alates are produced/released from their parental nest.

Alate "quality" is particularly important: heavy alates have higher survival when establishing a new colony (Cole et al. 2018; Cole and Rosengaus 2019) and mates with heavier partners have a higher probability of successfully establishing a new colony (Cole et al. 2018; Cole and Rosengaus 2019; Chouvenc 2019). Having ample energetic resources (i.e., mass) increases the probability that both queens and kings meet the competing demands between reproduction, immunity and all other important tasks required to the successful establishment of a new colony (Cole et al. 2018; Cole and Rosengaus 2019; Chouvenc 2019). Our models focuses on one general question:

While considering the contextual ecological setting, we ask if and when during the life cycle of a termite colony should TGIP be expressed in order to maximize colony fitness, defined above as maximizing alates produced over the life of the colony. In the current models, we assume that the focal individuals are capable of TGIP and we seek to identify the conditions under which its expression would be optimal.

Optimal decisions here are those that confer maximum lifetime reproductive success to a colony. In most instances, the latter is determined by offspring quality and quantity during the lifetime of the parent. We abstained from asking whether termite TGIP should evolve in the first place, as this question would require a different kind of analysis where a mutant, capable of TGIP, is introduced into a population lacking TGIP and then testing the conditions under which TGIP-capable mutants would become more prevalent. Given the incidence of TGIP across diverse taxonomic groups (Roth et al. 2018) and the recent report that eggs from immune-challenged *Zootermopsis* queens have more than double the number of RELISH transcripts relative to eggs from control queens (Cole et al. 2020a), we assume there are no genetic constraints to its evolution and thus, high performance TGIP strategies would have evolved (i.e., the phenotypic gambit—Grafen 1984).

This general question, in turn, stimulates discussion about additional scenarios worthwhile for consideration, including how the costs and benefits of TGIP, in combination with life-history attributes, ecological and evolutionary constraints, all combine to promote aspects of parental care that go well beyond parental behavior. That parents can influence the immune-competence of their progeny based on their own immune-status (i.e., in a context dependent fashion) represents a paradigm shift in our understanding of inheritance of acquired characteristics (Pigeault et al. 2016). Mapping the nature of TGIP against the backdrop of eusociality could provide new insights on the bidirectional impacts: how host/pathogen interactions influenced the evolution of sociality and how sociality may have ultimately, also influenced host/pathogen dynamics. To accomplish this, however, we require a theory that takes all of the above into account in a generalizable format. Thus, we ask the simple question: what should a theory of TGIP in eusocial insects look like? To answer this question, from our TGIP theory, we take two approaches, one where we include many life-history details and infection dynamics and the other in which we employ simple descriptors that disregard the nuances of colony-life. The simplified model still captures the spirit of the problem without incorporating finer details to generalize our approach. Below, we develop this resource-based TGIP theory.

Methods

Why use a state-dependent theory?

For this case study, we have chosen to develop a stochastic, dynamic state dependent theory. By state dependent, we

mean that the solution to how much (if at all, i.e., including nothing) parents should invest in TGIP, depends upon one or more state variables that describe the biology of a focal organism, and by state variable we mean some variable(s) that describes the state of a dynamic system. Imagine two colonies that differ in maturation state, one incipient colony (recently established) with little social structure complexity (few or no workers or soldiers) versus a mature colony with full and numerous representation of all castes, including future swarming reproductives (Fig. 3). It is easy to imagine that adaptive TGIP investment strategies will likely differ between such colonies just as they might for two human families, one young with small children and the other, mature, whose children are close to fledging. In this human analogy, we have now introduced the notion of context-dependent trade-offs as discussed above. Investing in one state (e.g., education state via dance lessons for the children) means that there are fewer resources for investing elsewhere (e.g., home improvement). The repercussions of such trade-offs may depend upon state (e.g., a rich versus a poor family). For termite colonies, we can capture colony structure (one state variable) and resource wealth (another state variable) at any one time as well as the colony maturation process via a dynamic state-dependent model. Below, we define and present each of the states in detail as well as their dynamics. A final point: when describing such dynamics it is important that we base ourselves on the actual biology of the focal organism, otherwise, this would simply be a mathematical exercise with little utility. Our theoretical approach includes and is based upon current empirical knowledge of termite pathobiology, physiological and communal immunology.

In addition to state dependence, we have chosen to include stochasticity in our theory as opposed to implementing a deterministic theory where events occur with some average probability each and every time. Important events (e.g., invasion of a pathogen) are generally stochastic in nature and their repercussions are likely state dependent. Again, returning to our young human family analogy, an unpredictable downturn in the stock market is likely to have a much greater impact on a poor versus a wealthy family or a young versus a mature family. Of course, such a downturn is predictable in the general sense but the exact timing is very difficult to predict and thus, our focal family should develop a suite of flexible state-dependent (i.e., context-dependent) responses to stock market events. In biology, we call such response suites phenotypic plasticity. As such, we assume that in one-piece termites, natural selection has honed plasticity in TGIP in a state-dependent manner in both the general sense (e.g., dangerous versus safe environments) and in specific response to particular stochastic events (e.g., spread of infection in a colony). It is this plastic TGIP strategy that we will address using well-developed techniques (e.g., Houston et al. 1988; Clark and Mangel 2000).

Although previous theoretical work on several aspects of TGIP and its dynamics already exists (e.g., Garnier et al. 2012; Pigeault et al. 2016), our framework differs from these others in various ways. Our models were constructed around empirically gathered characteristics of the pathobiology of termites that allow us to make focused predictions on the expression of TGIP in this and other eusocial taxa. The prior models are based on general concepts (e.g., dispersal distances, longevity) that facilitate generalized predictions. For example, though valuable in its own right, contrary to our theoretical framework here, the theoretical model by Garnier et al. (2012), was not state dependent nor did it incorporate population age or caste structure, which of course, are important features of eusocial organisms.

The current models can be described as follows. The focal colony is defined by its social structure at any given point in time (Supp. File 1, eq. S1); however, the model allows for such structure to change over time (Figs. 3, 4, 5 Supp. File 1, eq. S2) which in turn has subsequent impacts on queen performance (Fig. 6). Colony state is a dynamic variable as defined above and takes into account the number of individuals at each developmental stage and caste at any time, t. In addition, since we focus on colonies that live on a finite food source, we must also take into consideration the state (i.e., the amount) of resources at any time, t. Although wood quality is likely another important variable to consider, for simplicity sake, this variable was not included. Further, since there is some threat regarding risk from pathogens, we consider this risk both in the global sense (i.e., on average) and also locally, based upon the colony's knowledge of immediate risk. Thus, there is a knowledge state, whose value changes over time (Supp. File 1, eq. S9). In addition, we assumed pathogens are infectious and thus, the need to follow both infection states (i.e., who, in the colony, is infectious at any time, t; (Supp. File 1, eq. S7) as well as immunity state in order to determine if parents are selected to provide TGIP, or not. Finally, since we are interested in the adaptive nature of TGIP, we provide a stochastic dynamic programming methodology for evaluating how TGIP decisions impact colony fitness (Eq. 1, 2, 4).

Like any other deductive theory, ours has components consisting of facts (observational and experimental), assumptions and logical connectors. Moving beyond the broad-brush strokes employed above, we now describe in detail key features of our theory with and without the lens of TGIP as a comparison point. The formal models (Eq. 1, 2, 4) are shown below and subsumed equations can be found in Supplemental Material File 1.

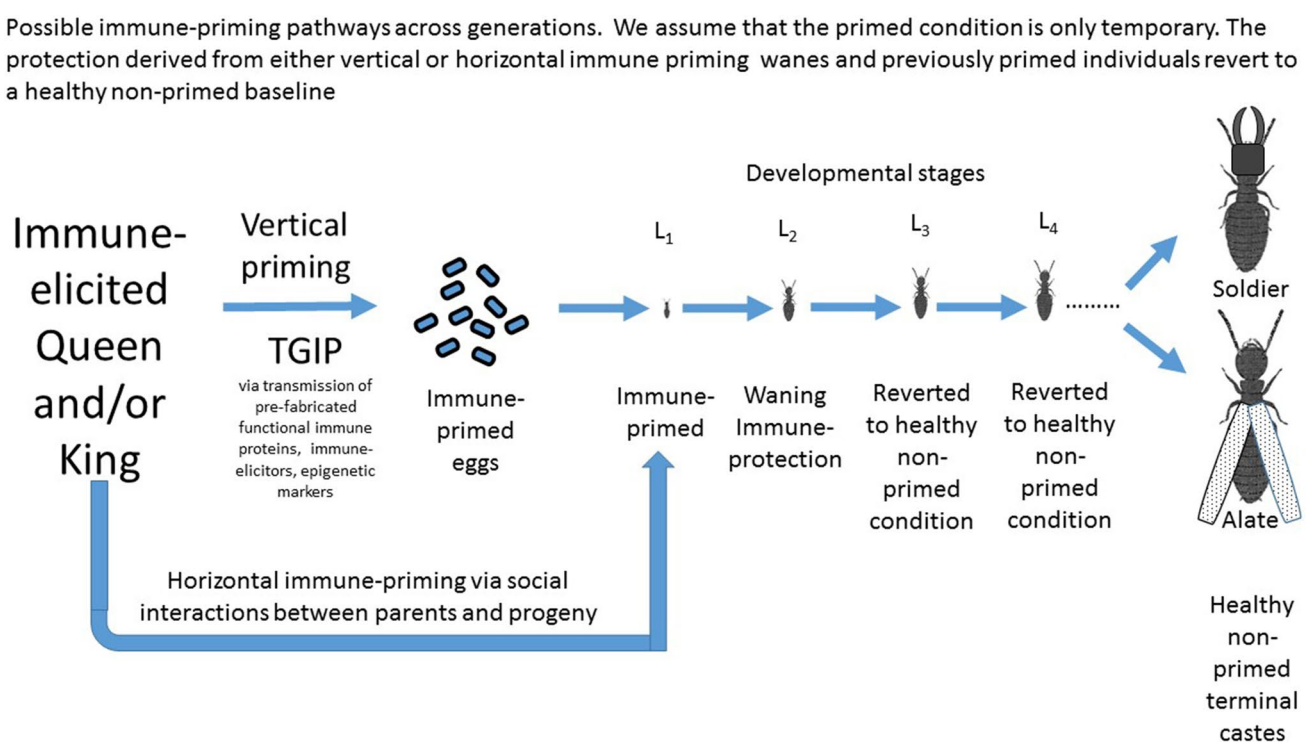

Fig. 4 Possible immune-priming paths across generations. We assume that the primed condition is only temporary; however, the point at which full reversion to healthy, non-primed baseline condition occurs will depend upon Transgenerational Immune Priming (TGIP) waning rate. If TGIP involves epigenetic inheritance, then the possibility exists that immune protection may never revert to the un-primed state

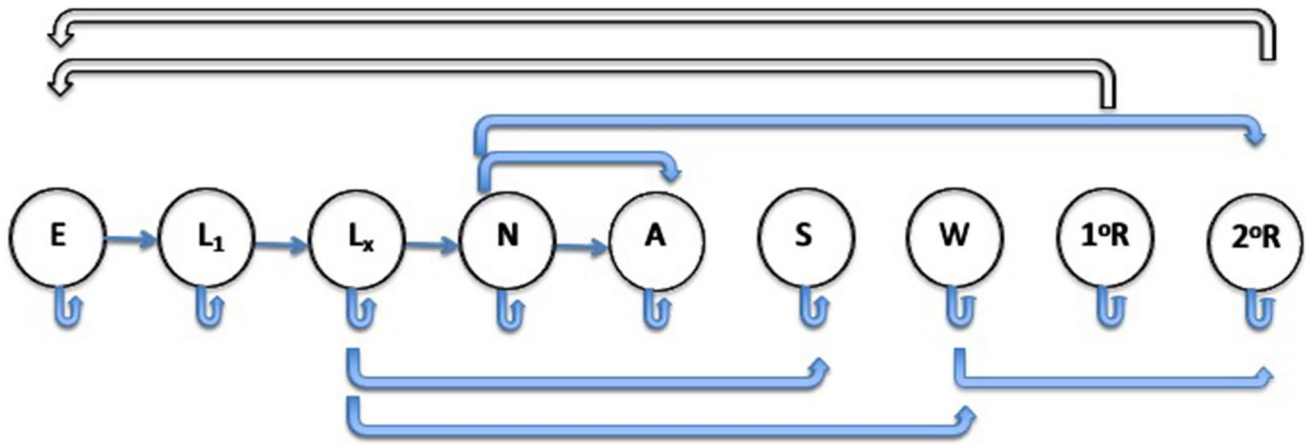

Fig. 5 Life diagram and corresponding transition matrix (Supp. File 1, eq. S2) for a termite colony. In the diagram, open arrows refer to contribution to the eggs via reproduction and solid arrows refer to contribution to caste or stage via either transition (i.e., molting) or non-transition (recursive arrow). The set of transitions shown in Fig. 5 for our theoretical colony, can be represented mathematically by a transition matrix (Caswell 2000; Supp. File 1, eq. S2). Unlike most other organisms, as shown in Fig. 5 and Supp. File eq. S1, termite larvae can contribute to several different castes

Nuanced (detail-rich) general model for adaptive TGIP

Assumptions

a) *The pathogen community of termites is variable across time and space.*

Prior to colony foundation, the swarming alates fall to the ground and move through the soil searching for a mate and an adequate nesting site. Given that diverse microbial communities colonize soils (many of which could be potentially pathogenic, Rosengaus et al. 2003; Tunaz and Stanley 2009; Ganesan et al. 2010; Soukup

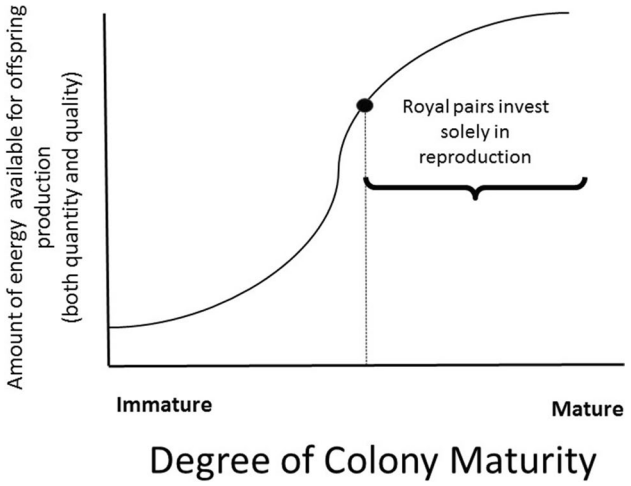

Fig. 6 Available levels of energy for reproduction by the royal pair as a function of the degree of maturation in the colony. Note that this energy can be invested in either increased numbers of offspring (quantity) or increased survival of progeny due to Transgenerational Immune Priming (TGIP) (quality). The circle denotes the point of the asymptotic curve where the royal pair emancipates from most colony labor. At this point, the progeny assumes all non-reproductives' responsibilities (i.e., nest maintenance, brood care, colony hygiene, colony-wide immunocompetence). Past this point, queens and kings rely on their functional brood to keep pathogens at bay through individual-level and societal-level immunity, reducing the parental need to engage in costly TGIP

et al. 2021), the now de-winged alates likely experience higher risks of infection during dispersal, construction of the initial nuptial chamber (copularium) and colony foundation than in the subsequent intermediate and mature stages of colony development (Fig. 3). During these later stages of colony development, reproductives move about the hygienically treated galleries, paved or fumigated with antimicrobial compounds produced and deposited by the colony's progeny (Rosengaus et al. 1998a, 2000a, 2004; Bulmer et al. 2009). Additionally, as the colony transitions into the intermediate and mature stages of development, the reproductives benefit from the intense allogrooming they receive from their functional brood (Fig. 3, Rosengaus and Traniello 1991) and thus, likely face lower pathogenic pressures. It is thus conceivable that pathogenic risks are highest during the earlier stages of colony foundation/development (Figs. 2 and 3), and such constraints may explain the high failure rates of young colonies (Rosengaus and Traniello 1993a; Hartke and Rosengaus 2013; Cole et al. 2018; Cole and Rosengaus 2019).

In our theory, we assume that there is some average background probability wherein at any time t, pathogen i, denoted, $\gamma_i(t)$, is present in the colony. In the section on Knowledge State below (IId), we explain how this global probability is translated to current assessment of the highly variable local risk via the queen's (and possibly the king's) sampling of her/their local environment. Further, in the section on Infection Dynamics (IIe), we explicate how colony structure/maturation level translates pathogen presence into infection rates. The expression of TGIP should not impact pathogen risk in the global sense, however, as shown below in Infection Dynamics (section IIe), it should instead impact infection rates via changes in immunocompetence.

b) *Pathogenic community of termites is variable with respect to species composition and loads*

As mentioned above, the different nesting, feeding and foraging ecologies across termites as well as overall habitat quality (Abe 1987; Rosengaus et al. 2003; Sorvari et al. 2008) places these social insects under different pathogenic constraints. Surveys of the microbial species richness colonizing either the termites' exoskeleton, guts, nests and/or their surroundings indicate that overall, they are colonized by diverse array of microbes (Hendee 1933, 1934; Sands 1969; Cruse 1998; Manjula et al. 2014, 2016; Arango et al. 2016; Chouvenc et al. 2018; Moreira et al. 2018; Soukup et al. 2021). Indeed, termites and their activities seem to foster the growth of certain microorganisms at the expense of others (Soukup et al. 2021). For example, termite presence is positively correlated with the presence and abundance of Rhizobiales and Actinobacteria while negatively associated with bacteria such as *Bacillus, Clostridium, Corynebacterium* and *Staphylococcus* (Chouvenc et al. 2018; Soukup et al. 2021). Moreover, the cuticular microbial loads vary significantly as a function of the species-specific nesting, feeding and foraging habits (Rosengaus et al. 2003). Based on the high abundance and diversity of the pathogenic community under which termites live, there is a high probability of simultaneous co-infection on a single host (see Eq. 1 and Supp. File 2).

It is noteworthy to recognize that some microbes are always pathogenic whereas others, such as S*erratia marcescens,* are opportunistic pathogens. *S. marcescens,* can live within the termites' gut with no negative impacts on the host; however, if it crosses the gut lumen into the body cavity, or if it enters the hemocoel via wounding, or if the termite is stressed in some other way, this relatively benign Gram negative bacterium can become pathogenic and cause host death (RBR personal observation; Mirabito and Rosengaus 2016 and references therein). Thus, when we refer to the impact of a given microbe i on its host (Ω_{ij}); see below), that impact depends upon the context (j) of its interaction with its host, described as $\gamma_i\Omega_{ij.}$

In the model formulation we first consider the general case where one or more pathogens may be perceived during one period of time (Eq. 1). Equation 1 includes

the probability that parents can be infected by one or more pathogens simultaneously while recognizing that the incidence of co-infection may be heavily dependent on pathogenic background levels and other ecological factors such as seasonality, degree of humidity, etc. These multiple pathogens might interact in various ways to influence termites, from strictly additive to synergistically and competitively (Supp. File 2). In the latter file, we provide methodology for including different kinds of interactions among multiple pathogens within a colony. To reduce model complexity, we consider the case where only one pathogen presents a risk to the focal colony (Eq. 2, 4).

As above, when viewed through the lens of TGIP, we do not expect change in global risk of pathogens, however, as shown below in Infection Dynamics (section IIe), TGIP should impact infection rates.

c) *Causes of mortality (μ_w)*: aside from colony collapse due to pathogens, colonies might also fail due to: (i) exhaustion of wood resource (the dynamic state variable, ρ, in Eq. 1, 2, 4), (ii) fire, (iii) drought, (iv) floods and (v) predators, among other factors. Further, we assume that the natural disasters occur at some rate that is independent of colony developmental stage. It follows that TGIP has no impact on these extrinsic pressures.

d) *TGIP is energetically costly.* We assume that expressing TGIP (τ) is costly and that the currency for investment in TGIP is measured in terms of reduced offspring (i.e., as TGIP investment increases there is a concomitant reduction in fertile progeny production). This is a key assumption. Recall, in Fig. 1, we assume that parents have a fixed amount of resources that they can invest in reproduction (η), thus TGIP investment decisions must be part of reproductive strategies. Figure 1 provides a contextual view of this key trade-off.

e) *Queens (and kings) are omniscient*—Critical to our theory regarding immune priming is that queens (and possibly kings) make adaptive TGIP decisions at least partly, based upon the maturation state of her (their) colony (Figs. 2, 3, and 6). We assume that the royal couple accurately tracks colony ontogeny via chemosensory cues from interactions with their subjects. There is a large body of insect literature supporting this assertion, including bees, ants and termites (Richard and Hunt 2013; Roitberg 2018; Yan and Leibig 2021).

Finally, this assumption holds whether viewed through the TGIP lens or not however, as omniscience is only critical when we assume that TGIP is present wherein TGIP shows phenotypic plasticity and depends upon knowledge of colony structure (Supp. File 1, eq. S1, S2).

f) *Immune priming: duration of protection may depend on the mode of priming*

Social insects provide a unique opportunity to think differently about TGIP and its protective consequences. By definition, TGIP refers to the vertical transmission of immune protection from parents to offspring via the germline. However, the reality is that eusocial insect parents, given their "intimate" and frequent social interactions with their progeny (mainly based on the exchange of bodily fluids), can potentially engage in the non-TGIP horizontal transfer of immune products that also function to protect their offspring (Traniello et al. 2002; Konrad et al. 2012). Behaviors such as mouth-to-mouth regurgitation (oral trophallaxis) or anus-to-mouth exchanges (proctodeal feedings, a common behavior in termites), can promote the transfer of functional prefabricated immune proteins and/or immune-elicitors that confer disease-resistance benefits to the progeny (Hamilton et al. 2010; Rosengaus et al. 2014, but see Mirabito and Rosengaus 2016) and/or epigenetically. This horizontal transfer of immune function could be as effective as TGIP. Clearly, both vertical (TGIP) and horizontal transmission of immune function among nestmates can be complimentary. The only added benefit of vertical over horizontal transmission is that through TGIP, parents can add relatively inexpensive epigenetic markers to their unborn progeny, potentially altering the offspring's immune-gene expression across multiple generations (Gegner et al. 2009; Mondotte et al. 2020). These alternative mechanisms of immune priming (vertical vs. horizontal, or epigenetic vs. functional prefabricated immune proteins/immune elicitors) likely have important consequences on the duration of such "primed" status in subsequent generations. We assume that horizontal or vertical transfer involving prefabricated functional immune proteins or immune-elicitors likely provide relatively short-lived benefits, given that the transferred immune-effectors and compounds have higher risks of becoming denatured in the external environment or broken-down by the recipients' metabolism. On the other hand, epigenetic modifications could result in longer-term immune benefits, spanning multiple generations (Mondotte et al. 2020). Whether vertical or horizontal immune-priming via the transfer of functional effectors and/or immune-elicitors, the expectation is that primed offspring should at some point revert to a healthy un-primed baseline (Fig. 4). Hence, while infected individuals can revert to a healthy state after generating a successful immune response, immune-primed individuals can revert to a healthy-unprimed status. Potentially, the epigenetic alterations of progeny's DNA could also revert to the baseline state as long as the progeny's DNA epigenetic markers return to their original state (for example, progeny's DNA becomes un-methylated and/or its histones become un-acetylated).

We assume that queens can choose to prime eggs and/or larvae based upon maximizing alate production over the lifetime of the colony (see formal model below; and in Fig. 4).

We further assume that enhanced immunity wanes over time after TGIP has been elicited wherein the rate of such decline depends upon the type of priming as discussed above (see Infection Dynamics (IIe) for details and Fig. 4 below). Given sufficient time, a TGIP individual would appear identical to a non-primed individual.

g) *Individuals may recover from infection*—Hosts that experienced "recovery", by definition, require that, regardless of developmental stage or caste, they are successfully invaded by the pathogen which subsequently elicits an effective immune response by the host. Such immune-elicitation results in the deactivation of the pathogen and the continued survival of the individual, who has now attained the status of "recovered". The "recovered" individual may have (or not) exhibited symptoms of disease (such as lethargy or anorexia; Rosengaus and Traniello 1997; Adamo et al. 2010; Sullivan et al. 2016), but ultimately, the host returns back to a healthy and fully functional status (see Infection Dynamics, section IIe and Fig. 4). Note, priming is not 100% effective; we assume that some primed individuals will become infected and some portion of them will recover though not necessarily at the same rate as non-primed individuals.

Dynamic state variables We describe a termite colony as a function of different "states." Such states are based on known basic extrinsic (i.e., environmental) and intrinsic (i.e., biological) characteristics of basal termites (Table 1) and their possible interactions. Notably, we recognize that this list is not exhaustive and that other factors missing in our current model may also influence the expression of TGIP, its magnitude, its protective duration and adaptive value across subsequent generations. Yet, the included extrinsic and intrinsic states should provide a realistic approximation to the questions of when during the life cycle of a termite colony, should TGIP be expressed, and what kinds of TGIP are optimal. Each extrinsic and intrinsic dynamic state below presents first, an overview of its biological significance followed by a description of how the expression of TGIP likely modulates it.

Extrinsic state

a) *Wood resources (referred to by the symbol "ρ") are highly variable and change as a function of colony size and colony age.* In nature, swarming alates have to contend with variable and unpredictable wood resources as they hurriedly choose their nesting and feeding site to escape predators and avoid desiccation. Although some termite species feed on humus, soil, grasses and fungi, the majority feed on dead fallen logs that vary in diameter, length, degree of decomposition, palatability, hardness and overall nutritional quality (Evans et al. 2005). The alates' initial decisions on which log to establish a colony will determine, in large part, the size, growth rates and life expectancy of the future colony. Furthermore, termites use vibroacoustic signals to assess the amount of available wood which in turn, influence the differentiation of larvae into neotenic reproductives (Evans et al. 2005). Therefore, the initial wood selection made by alates can sustain their colony for decades and ultimately, influence overall colony fitness. Regarding one-piece termites, their colonies spend their entire lives within a piece of wood that provides both food and shelter (Abe 1987). Inevitably, this resource must decline over time (i.e., it is dynamic).

In our theory, we only consider how, once chosen, colony-site selection might influence the expression of TGIP. In other words, we consider TGIP decisions for a colony that finds itself already at a given wood resource. Additionally, at the incipient colony stage (Fig. 3), negligible amounts of wood are consumed by the king and queen. At intermediate and mature colony stages (Fig. 3), however, we assume that workers consume wood at constant per capita rate until wood is ultimately, fully consumed. At this point, the colony dies (i.e., colony fitness can be described by a step function).

Though it may seem counterintuitive, we expect that the wood resource will decline at an increased rate after TGIP is expressed. While it is true that queens sacrifice progeny production (η) for TGIP (τ) (i.e., they reduce offspring quantity, η-τ) (Fig. 1), they gain from increased offspring survivorship (quality). This trade-off results in higher colony productivity overall and, as such, a faster exploitation of the non-renewable wood resource.

Intrinsic states

a) *Nest demographic composition (c)*

The demographic characteristics of a social insect colony, such as its age structure and/or caste composition are of paramount importance for securing not only the necessary resources but also play a role in constructing, maintaining and/or improving the nest structure, performing brood and reproductive-caste care as well as defending the colony against predators and, most relevant to this work, pathogens. The successful and efficient use of energy to accomplish all these tasks increase colony fitness (Oster and Wilson 1979). Within the context of disease resistance, theoretical and empirical evidence across several eusocial insect taxa indicate that the number of individuals, their developmental stage (i.e., chronological age) as well as caste composition within the colony, significantly influence survival

Table 1 List of states that potentially influence the expression of Transgenerational Immune Priming (TGIP)*

	Life history traits	Incipient stage	Intermediate stage	Mature stage
Extrinsic (to the colony) factors	Resource availability (wood for feeding/ nesting)	High	High	Low
	Pathogenic risk due to nesting, feeding and foraging ecologies	High in species that establish their incipient colonies within decayed wood or underground	High in species that remain nesting/feeding/ foraging within soil and/or decayed wood Lower in species that build arboreal nests and/or build mounds	Low in species that remain nesting/feeding/ foraging within soil and/or decayed wood since these substrates have been treated with termite-derived antimicrobials Low in species that nest/forage in arboreal setting and/or build mounds as these sites have lower microbial loads and lower microbial diversity than ground dwelling
	Pathogenic load (stochastic variable)	Very high (during swarming, tandem running, locating new nesting site, mating)	High (during construction of copularium and nest expansion)	Low (nest and food source are now covered with antimicrobial compounds)
	Pathogenic diversity	High (a myriad of bacterial, fungal, viruses, nematodes)	Intermediate	Low (nest/food has a less diverse microbial community after being treated with termite-derived biochemical secretions)
Intrinsic (to the colony) factors	Infection state	Highest	Intermediate	Lowest
	Energetic reserves of reproductives	Lowest	Intermediate	Highest
	Conflicting demands with immune system	Many (gametogenesis, courtship, mating, copularium construction, nest hygiene, oviposition, brood care)	Multiple (yet fewer than incipient stage) (gametogenesis, mating, nest hygiene, nest expansion, oviposition, brood care)	Minimal conflicting demands except for reproduction (no brood care, no nest construction)
	Colony structure	Low (simple age cohort structure	Intermediate structure	Complex (multi-age and multi-caste) structure
	Resiliency against stochastic events	Least resilient Resilience is constrained given their little ability to cope with unexpected environmental stressors	Intermediate resilience to stochastic events	Most resilient given that mature colonies have a higher potential for mediating stochastic events

* This list includes several aspects of termite biology that could have served as possible preadaptations for the origins and maintenance of TGIP in the termite ancestors. Although this is not an exhaustive list, identifying these extrinsic and intrinsic factors, most of which have empirical backing, results in an integrative approach that fuses both empirical and theoretical perspectives

(Rosengaus et al. 1998b; Rosengaus and Traniello 2001; Fefferman et al. 2007; Wilson-Rich et al. 2008; Castella et al. 2010; Bull et al. 2012). The investment that parents make on their sterile workforce can alter the dynamics and eventual outcomes of pathogenic exposure (Cole et al. 2018; Cole and Rosengaus 2019, 2020b; Fig. 1). Notably, theoretical work also indicates that longer-lived hosts, such as termites (Thorne et al. 2002), are more likely to exhibit heightened juvenile susceptibility to infection relative to hosts with shorter life-spans. This in turn, increases disease spread and prevalence (Ashby and Bruns 2018) supporting our proposal that social structure of a eusocial insect colony heavily influences disease spread and prevalence and therefore, affects the expression, magnitude and duration of TGIP. We have evidence that older *Z. angusticollis* termites are less susceptible to mycosis by the entomopathogenic fungus *Metarhizium* than younger nestmates (Rosengaus and Traniello 2001) and that termites maintained in mixed-age groups exhibited significantly lower mortality due to mycosis than isolated or same-age grouped individuals (Rosengaus and Traniello 2001). These results point to emergent social benefits against disease that likely arise from diverse age-based immune function and/or different age-based hygienic task specialization (see Section IIc below). We argue that in a termite colony, the investment that parents make toward colony growth (i.e., progeny's density, age distribution and caste composition; all subsumed under Social Structure (SS) in Fig. 1), play a significant role in a colony's disease control capabilities (BIC in Fig. 1) and consequently, in the maximization of that colony's fitness.

Termite colonies are typically comprised by a number of individuals in each developmental stage and caste: egg (E_1, E_2, E_3 as defined by Cole et al. 2020b), larvae (L_1,$L_{2....}L_x$), nymphs (N_1, N_2), alate (A), soldier (S), functional pseudergate worker (W), primary (1°R) and secondary reproductive (2°R), respectively (Fig. 5). For simplicity-sake, in this model we only include just one egg stage and one nymph stage. When stages vary in their survivorship and fecundity, as is the case here, it is appropriate to describe the colony by a time-dependent stage distribution vector (Caswell 2000; Neubert and Caswell 2000; Supp. File 1, eq. S1) where the number of individuals in each stage is represented by an element in its own row.

Now that we have defined the different developmental stages, it is important to understand how colony demography and the transitions between subsequent developmental stages or into different terminal castes play a role in pathogen-related social interactions, individual survival given infections and ultimately, colony fitness. Hence, we must now describe the transition of individuals from one stage to the next, including non-transition during some predefined period of time. For practical purposes, we have defined time as passing in discrete, three-day periods. Periods shorter than three days are unlikely to have any significant and meaningful change regarding the progress of pathogens, and periods greater than a week are likely to contain many meaningful changes. Thus, based on existing empirical termite research, 3 days is a practical, useful, and biologically relevant unit of time.

We illustrate the transitions of the various instars and castes within a colony, in a flow diagram and corresponding transition matrix (Supp. File 1, eq. S2; Fig. 5). In this example, we only show two of the possible six larval stages. The solid arrows indicate contribution via transitions and non-transitions, including stationary molts (which may occur in *Zootermopsis* and other termites; Korb et al. 2021). The open arrows show contribution via reproduction (i.e., production of eggs).

The transition matrix includes mortality (Supp. File 1, eq. S3) during transition. In addition, note that there is no recruitment of primary reproductives after colony establishment (although instances of colony merging may actually occur in nature). Finally, although the possibility exists that regressive molts (e.g., a fifth instar becoming a fourth instar after its molt) happen in this species, it is sufficiently rare that we have chosen not to include this phenomenon in this matrix (Korb et al. 2021).

Note that the elements in our transition matrix (Supp. File 1, eq. S2) are shown here as constants whereas, in reality and below, we use them as functions. For example, primary reproductive fecundity varies with colony maturity. As the colony matures, the queen becomes emancipated from housekeeping duties and focuses her energy solely on producing offspring (Fig. 6). Similarly, survivorship is also a function whose value will vary locally depending on pathogen presence and immunocompetence, which can vary and is discussed below.

From the perspective of TGIP, we assume realized fecundity of queens to be reduced as they invest in TGIP (see top row of the transition matrix (Supp. File 1, eq. S2) and described earlier as, η-τ, which are equivalent in this case). In addition, all of the non-zero survivorship terms will be functions of expected pathogen risk and increased immunity from TGIP, if expressed. We discuss these functions in detail in the Supplemental File 1 and, in particular in the Infection Dynamics section below (IIe).

b) *Colony ontogeny*

The chronological age of a termite colony may influence its susceptibility to disease and consequently, the incidence and magnitude of the benefits accrued from expression of TGIP. This is not necessarily because older colonies (if age is measured from the moment of colony establishment) are more competent in their physiological immune responses, but rather because older colonies are likely to benefit from the social facilitation of disease resistance (Rosengaus and

Traniello 2001; Traniello et al. 2002) and social immunity (Cremer et al. 2007, 2018; Cotter and Kilner 2010; Meunier 2015) to a greater extent than younger colonies. In termites (and other eusocial insects), the ontogeny of sociality is fundamentally confounded with chronological colony age, overall density, demographic composition (age and caste composition) and social interactions. The fusion of all these multiple variables likely results in emergent disease-resistance properties at the societal level and this makes eusocial insects unique relative to other solitary and social species. In the latter, the dynamics of infection as a function of their sociality is likely coupled with chronological age, overall group density, demographic structure and reproductive potential to a lesser degree than in eusocial insects. We view colony structure as a continual maturation process. However, in termites, we can distinguish at least three basic yet discrete stages in this developmental continuum:

(i) Incipient stage of colony foundation (Fig. 3; Supp. File 1, eq. S4.1) (defined here as containing one or both reproductives with their first brood (mainly eggs) but no functional workers or soldiers.

(ii) Intermediate stage (Fig. 3; Supp. File 1, eq. S4.2) consists of one or two members of the royal pair accompanied by eggs of different embryological stages (E1-E3; Cole et al. 2020b), multiple larvae of different instars (I–VI) and a few miniature soldiers. At this intermediate stage, the royal pair is still heavily involved in egg and young larval care (instars I–II) while older instars (III and older) initiate brood- and royal-care activities as well as nest maintenance (Rosengaus and Traniello 1993b; Crosland et al. 1997).

(iii) Mature colony stage (Fig. 3; Supp. File 1, eq. S4.3) consisting of one, both or none of the primary reproductives, and in their absence, one or multiple supplementary reproductives (neotenic or ergatoid), eggs, hundreds to thousands of larvae of different instars, numerous nymphs and soldiers with massive heads (as compared to the miniature soldiers of the intermediate-age colonies). At this mature stage, individuals ranging across the third to the nymph instars, function as a single functional workforce (pseudergates), specializing in brood care, royal care and colony enlargement/maintenance (Rosengaus and Traniello 1993b) while retaining the potential for attaining reproductive status. Somewhere along the intermediate and mature stages of colony development, the original reproductive caste (if still alive) or supplementary reproductives reach the point where they become emancipated from brood care and solely specialize on reproduction (Fig. 6). In other words, the reproductives at this stage have irreversibly transferred all colony-related duties (except mating and reproduction) to their progeny (Chouvenc and Su 2017). Mature colonies, by definition, release winged individuals (alates) that swarm away from their natal nest to establish new colonies (Fig. 3).

Defining colonies in this admittedly artificial three-step ontogenetic progression along the natural continuum of the life cycle of a termite colony is useful as we attempt to establish the impact that disease has on the potential expression of TGIP.

iii) Immunocompetence at the colony level (ζ)

We define colony level immunocompetence as an emergent property of individual immunity along with social interaction among nestmates that further confer resistance to infection. Individual immune function includes physiological response such as phagocytosis of the pathogen by host hemocytes (Avulova and Rosengaus 2011), activation of the phenoloxidase cascade (Rosengaus and Reichheld 2016), encapsulation (Calleri et al. 2007), and/or the upregulation of antimicrobial peptides circulating the insects' hemocoel (Rosengaus et al. 1999, 2007), all of which can ultimately render the pathogen inactive.

Colony immunocompetence is defined as a vector akin to the age distribution vector above (Supp. File 1, eq. S1) but, for each stage (with attributes corresponding to each specific caste and instar), there is an average level of caste- and age-specific immunocompetence c_i which is a function of a) personal physiological immunity (which contributes to herd immunity) and b) social facilitation of disease resistance and/or colony-wide immunocompetence which in turn, is the sum of the individuals allogrooming, secretions and nest hygiene. Thus, colony-wide immunocompetence depends on several functions, including: (i) the number of members in each caste, (ii) the age composition of the group, (iii) behavioral and biochemical mechanisms to resist disease via social interactions (pathogen alarm response, allogrooming) and/or deposition of termite-derived antimicrobial compounds (Rosengaus et al. 1998a, 2000a, 2004).

Colony-wide immunocompetence (ζ_C) (Supp. File 1, eq. S5) for a colony of size N with a given stage structure as defined above (Supp. File 1, eq. S1), can be calculated by summing across the colony's stage distribution vector and weighting each stage, by its relative representation in the colony and its stage specific social-immune contribution.

For example, a young colony that is largely composed of eggs and young larvae who contribute little to colony-wide immunocompetence, will have an ζ_C score close to zero whereas a colony that is worker heavy will have a ζ_C score close to 1. In the Infection Dynamics section below (IIe), we show that the risk from pathogens depends upon colony-wide immunocompetence, which in turn, depends upon colony caste and stage structure.

In addition to the above, there is indication that within-colony demographic diversity, in of itself, can impact disease resistance at the colony level (Rosengaus et al. 1998b; Rosengaus and Traniello 2001). To capture this effect, we introduce a modifier term, ε (Supp. File 1, eq. S6), that varies from 0 to 1 and may be recognized as something akin to Simpson's diversity index (Simpson 1949). Thus, the higher the caste diversity, the greater the realized colony-level immunocompetence (i.e., lower susceptibility generated by ε).

When TGIP is in play, we consider two types of individuals, those that are primed and those that are immunologically "naïve." We assume that susceptibility to pathogens is always lower for primed individuals. This is made explicit in the Infection Dynamics section below (IIe) and, in particular, equations (Supp. File 1, eq. S11, S12, S19).

iv) Infection State (ω)

To make predictions on the nature of TGIP, its duration and its adaptive value (i.e., its impacts on colony fitness), we need to understand the dynamics of infection within a colony (Fig. 7), which we know are significantly influenced by the degree of colony maturation, caste composition, age distribution, pathogenic loads and the probability of coinfection. We thus use the infection state to describe the sum total of infection within the colony as a function of its maturational state and its subsumed demographic (age and caste) composition; see rows in (Supp. File 1, eq. S7). When multiple pathogens have infected the colony, the infection matrix would be composed of extra columns, one per pathogen (see Supp. File 1, eq. S8).

The dynamics of infection state are complicated. They can be best illustrated by focusing on a single cell in the matrix (Supp File 1, eq. S7 that is also depicted in Fig. 7). For example, the proportion of alates (A) at time = t + 1 who are infected by a pathogen, is determined by: the value of A, at t, multiplied by the proportion who survive (as alates) (and do not transition, i.e., a_{AA}) plus the proportion of healthy alates at t who survive and become infected by the pathogen. In addition, we need to consider L_i individuals at time t who eventually (after undergoing several additional molts) transition to the nymph and then alate caste who are already infected by the pathogen as well as healthy L_x transitioning individuals who become infected during time t. This is made explicit in the Infection Dynamics below.

As to the probability of an individual belonging to one instar becoming infected by a particular pathogen, that depends upon its immunocompetence, its interactions with other individuals from different castes or other instars, the infection level within each caste/instar and pathogenicity of the various pathogens, which may be driven by interactions among pathogens (see Supp. File 2). We flesh out the details of these critical interactions in the Infection dynamics sub-model (section IIe) below. Before we can do so, however, we need to contextualize these dynamics from the queen (and king's) perspective since they must 'decide' whether to deploy TGIP. This is explained in the Knowledge State section immediately below.

Finally, regarding TGIP, we can expect that increased immunity from TGIP will impact infection dynamics by altering rates of transition between healthy and infected states. We detail these changes in the section on Infections Dynamics, with and without TGIP.

e) *Knowledge state (Q)*—We assume that the queen and king monitor their environment for pathogens as they move through the nest galleries, mostly via olfactory cues as this is the primary sensory mode for arthropods (Rosengaus et al. 2000b; Yanagawa et al. 2009, 2015; Mburu et al. 2011; Roitberg 2018). Exposure to pathogen odor elicits a physiological and/or behavioral change

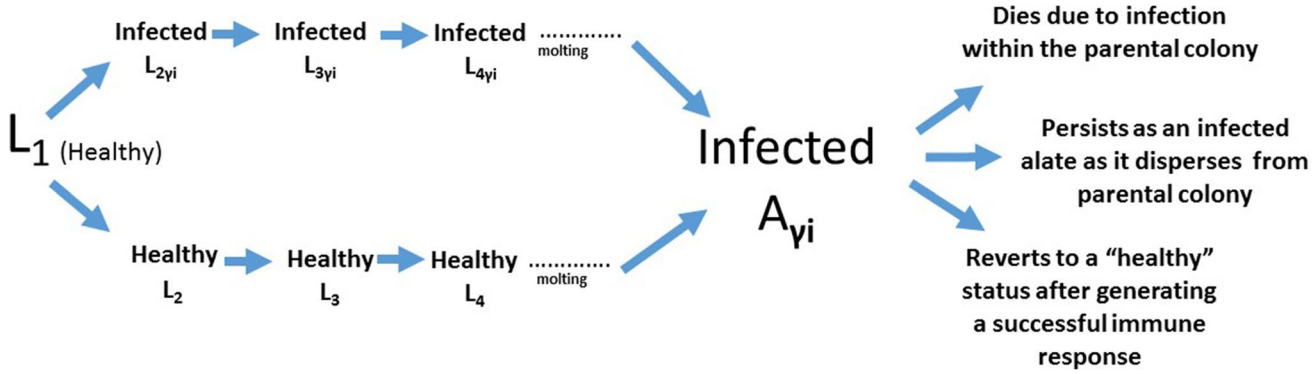

Fig. 7 Potential infection dynamics that can occur as a hemimetabolous individual ages within a colony. This example is taken from larva larva instar 1. This figure should be interpreted along with Supp File 1, eq. S7. Healthy individuals can remain unexposed (and thus healthy) throughout their development (instars) or can attain an infected status which is maintained across several instars. Once a terminal instar is reached (either soldier or alate), the infected individual has several options: to die of infection, persist as an infected terminal instar or revert to a healthy status following a successful immune response

in TGIP expression akin to physiological responses that termite larvae (and workers of other social insects) undergo under the influence of queen pheromones, which are emitted to regulate the colony's social structure (Matsuura et al. 2010; Himuro et al. 2011; Holman 2018). The queen and/or king estimate(s) the risk to offspring from the locally unpredictable microorganisms colonizing their environment. The parental estimation of pathogenic risk is a key feature of our model because it connects current parental assessment of pathogenic risk to future offspring immunocompetence through TGIP.

To capture this phenomenon (Supp. File 1, eq. S9), we assume that parents arrive at their new colony site with some inherited knowledge of pathogen risk, based on global average. This initial knowledge state may be referred to as the "known and likely anticipated" estimate of risk to offspring, or prior, in the vernacular of Bayesian theory (Mangel 2006; McNamara et al. 2006). Each time the queen/king sample(s) anew her/their local environment for pathogens, the updated risk value is combined with the aforementioned "known" current risk to generate a new updated or posterior value, which can then be used to determine the appropriate TGIP response. We assume that the queen (with possible contributions from the king) updates her pathogen estimate, once per time period t, throughout her life, each time generating a new posterior, which becomes her new information state. Note that this updated state value may be higher or lower than the prior, depending upon whether the queen perceives the presence of a pathogen or not, respectively. Thus, over time, the queen's (less-than-perfect) estimate of pathogen risk to her offspring will vary and, at the onset of each time period, she will need to make the adaptive decision whether to engage in TGIP.

Ability to express TGIP should have no impact on knowledge state since pathogen presence is independent of the queen's ability to mediate its impact.

Given the queen (and king's) knowledge state, we can now calculate her/their estimate of infection within the colony on a per stage basis.

f) Infection dynamics

We describe the infection dynamics using a variation of the classic SIR model (Kermack and McKendrick1927) (Supp. File 1, eq. S10), in discrete time, where "S" refers to Susceptible, "I" refers to Infected and Infectious and "R" refers to recovered. Individuals transition between these three classes based upon transmission rates, susceptibility, recovery rates, etc. Because a termite colony is structured on the basis of its inherent caste and age demographics, we must compute the dynamics for each caste and each instar (represented by successive stages in the stage vector Supp. File 1, eq. S1). We assume the following:

I. Individuals may encounter and may be attacked by free-living pathogens who are present within the nest wherein the probability of such events depends upon

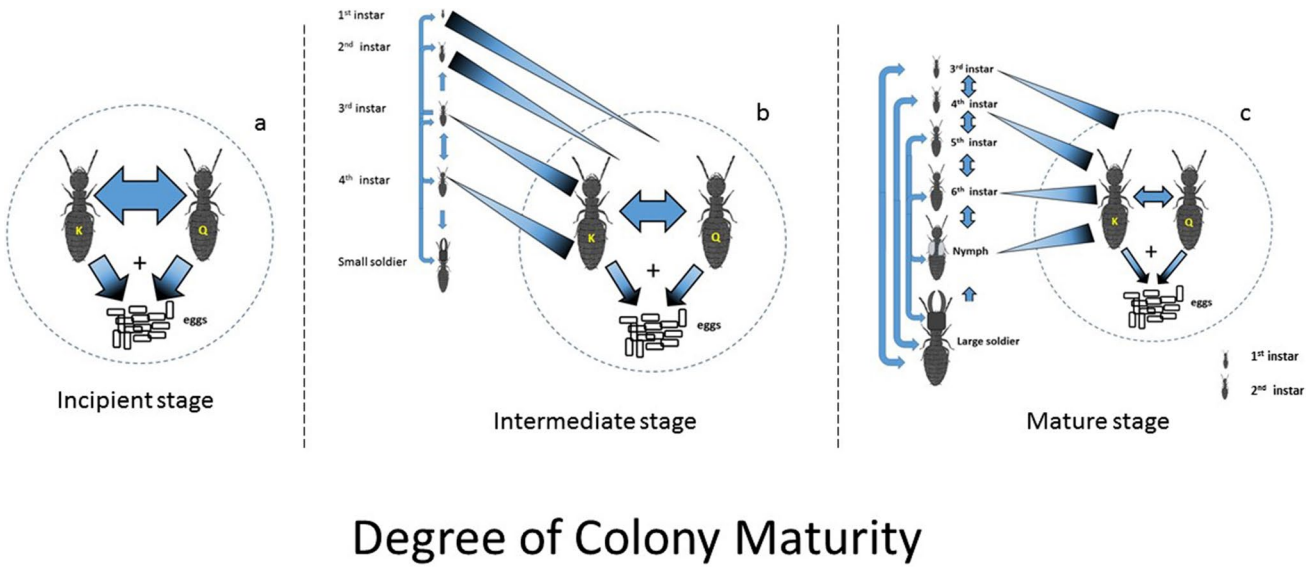

Fig. 8 Relative rates of social interactions and their concomitant risks of horizontal infection (due to the social interactions among colony members) as a function of the degree of colony maturation. The arrow thickness and direction correlate with the frequency with which social interactions are performed toward a particular developmental stage (eggs, larvae, nymphs, soldiers). The graded darker coloration indicates higher frequency of social interactions toward that individual. The social dynamics depicted in this figure are substantiated by results from Rosengaus and Traniello (1991, 1993b)

caste/age specific immunity and colony-wide immunocompetence as described above (section IIc),

II. Individuals may encounter and may be attacked by pathogens during interactions with other nestmates (see Fig. 8).
III. Note that the set of interactions differ depending upon the maturity level of the colony, caste and age distribution (instars) as noted in section IIc on immunocompetence. Note also, though not explicit in a mechanistic sense, the probability of infection from such interactions also includes the social benefits from such interactions on a caste-per-caste or instar-per-instar basis.
IV. Infection fully develops within a single time period (i.e., there is no latency or incubation).
V. The dynamics can be described in discrete time. For example, as above, we can compute the probability that individual alate might be infected by the focal pathogen during a three-day period (Fig. 7; Supp. File 1, eq. S10).
VI. Individuals recruit in and out of each developmental stage via the normal maturation processes (Supp. File 1, eq. S2).

A brief description of the SIR dynamics follows.

Healthy and susceptible: The number of "susceptible individuals (S)" at a given instar or caste depends upon healthy individuals recruiting in and out from younger and older stages, respectively, plus those individuals that "recovered", who have lost their partial immunity minus "healthies" that become infected by interacting with infected nestmates minus those that become infected from the background pathogen load in the environment minus any susceptible individuals who die of natural causes other than the disease agent.

Infected and infectious: The number of "infected" individuals (I) at a given instar or caste depends upon infected individuals recruiting in and out from younger and older stages, respectively plus healthies that become infected by interacting with infected nestmates plus those that become infected from the background pathogen load in the environment minus those that "recover" from infection (λ) minus those that transitioned to the next instar or caste (a_{c+1c}) minus those that die from the pathogen minus those "infected" individuals who die of natural causes other than the disease agent.

Recovered: The number of "recovered" individuals (R) at a given instar/caste depends upon recovered individuals recruiting in and out from younger and older stages, respectively plus those that recover from infection within the previous time period minus those that lost their limited immunity minus those "recovered" termites who die of natural causes other than the disease agent.

Now that the different outcomes of an infection have been presented (Supp. File 1, eq. S10 above), we turn our attention to TGIP. It is important to note here that the infection dynamics detailed below are, in fact, expected infection dynamics, based upon the primary reproductives' knowledge of the local pathogen community. We modified our initial SIR by adding a class, which is comprised of individuals who have been primed "vertically" as eggs produced by the queen, through the germline (either through the contribution of prefabricated immune-related proteins, transfer of immune-elicitors or epigenetic markers) to reduce their susceptibility to infection or "horizontally" while in larval stage. In addition, primed immunity wanes at some rate wherein primed individuals return to become healthy and potentially susceptible, S. Note that egg and larvae, respectively, are the only castes that receive vertical (TGIP) or horizontal priming from the queen/king. These modifications move us from the classic 3-equation SIR model to a six-equation one that now includes TGI-primed and unprimed individuals within each of the S, I and R classes (see Supp. File 1, eq. S11).

The dynamic state variable model for adaptive TGIP In the discussion above, we explained our logic for including a number of parameters in a model of TGIP expression for a colony of one-piece nesting termites. Below is the formal dynamic state variable model that integrates all these parameters. What we seek here are conditions under which TGIP would be adaptive, given the infection dynamics defined earlier. Recall that we assume that queens have the ability to provide TGIP when they deem it beneficial to do so.

Here, we assume there is risk from a single pathogen γ_i, however, the model could easily be expanded to accommodate more types of pathogens (see Supp. File 2). We provide a table of the model terms and their meaning in Table 2.

Our dynamic state variable model is shown below for the general case with more than one pathogen species possibly present.

$$F(\rho,c,\psi,\chi,Q,t,T)=\max\tau\ \eta(c,\tau)\mu_{\mathrm{f}}^{\alpha}+\mu_{w}\left[\begin{array}{c}\prod_{i=1}^{P}(1-\gamma_i)F(\rho',c',\psi',\chi',Q',t+1,T)+\\ \left(1-\prod_{i=1}^{P}(1-\gamma_i)\right)F(\rho',c',\psi',\chi',Q'',t+1,T)\end{array}\right] \quad (1)$$

Table 2 Terms and their meaning for two dynamic state variable models (Eq. 1, 2, 4; Supp. File 1, Eq. 11 and 12) for TGIP decisions in a one-piece termite colony

Term	Interpretation
F	Expected lifetime fitness from alate production
ρ	Wood resource state
c	Colony caste structure – a vector of the number of individuals per stage
ψ	Colony infection state – a vector of the proportion of infected individuals per stage
χ	Colony immune state – a vector of the immune level of individuals per stage
Q	The queen's estimate of the probability that a pathogen is present at the colony
η	Number of alates produced during period t
τ	Queen's investment in TGIP (in potential offspring units)
$\gamma_{i,}$	Probability that a pathogen is present
μ_f	Survival rate for progeny destined to be alates from non-pathogen risk of mortality
μ_w	Survival rate for the colony from non-pathogen risk of mortality
T	Maximum length of reproductive life

The way to read the model from left to right is as follows: The expected fitness (F) for a colony with wood resources ρ, composition and size c (a vector), infection state ψ (a vector), immune state χ (a vector) and knowledge state Q at time t with a maximum lifespan of T is equal to: fitness from production of alates (discounted by the product of survival rate and the time it takes to become an alate), η, as a function of colony composition and size and investment in TGIP, plus future production discounted by the probability invasion by the focal pathogen and non-pathogen threats. This expected future production depends upon whether the queen perceives presence of the focal pathogen. If so, no pathogen is perceived with probability $\prod_{i=1}^{P}(1-\gamma_i)$ and discounted by the probability of surviving into the future given non-pathogen mortality factors (e.g., floods) μ_w, the colony can expect future production of alates, dependent upon the updated state variables, in particular, expected increased risk regarding pathogens. If at least one pathogen is perceived with probability $1-\prod_{i=1}^{P}(1-\gamma_i)$, then similar calculation is required but with a different new knowledge state, Q" wherein expected risk from pathogens is greater than above. Note the max term signifies that the queen should choose the level of TGIP (τ) that maximizes expected lifetime alate production at the expense of current alate production due to investment in TGIP. Also, note the primes attached to the state variables on the right hand side signify that each of them has changed either via passage of time and ensuing dynamics or, for the knowledge state, via encounters (or not) with pathogens. Finally, note the knowledge state, Q, should differ for the two possible events thus they receive different numbers of primes.

For our special case where we have assumed, just one pathogen species, the model reduces to:

$$F(\rho,c,\psi,\chi,Q,t,T)=\max_{\tau}\ \eta(c,\tau)\mu_f^{\alpha}+\mu_w\begin{bmatrix}(1-\gamma_i)F(\rho',c',\psi',\chi',Q',t+1,T)+\\ \gamma_i F(\rho',c',\psi',\chi',Q'',t+1,T)\end{bmatrix} \quad (2)$$

Finally, note that when t = T (the maximum lifespan of a reproductive) or when ρ = 0 (resources are exhausted), future fitness of the colony = 0, i.e., F(ρ,c,ψ,χ,κ,t,T) = 0 (Eq. 3). Also, note that ρ(t) is always greater than ρ(t + x) wherein the finite wood resource is consumed over time.

Simplified (detail-lean) general model for adaptive TGIP

In this section, we move from our detail-rich model of TGIP to a more general, detail-lean model that still captures the key features of adaptive, plastic TGIP, namely, (i) it is resource driven, (ii) it works across small and large timescales, and (iii) it connects parent's experience to offspring performance. We accomplish this by replacing our complex sub-models with simple functions.

First, we replace the colony-structure matrices with a single metric, M, maturation state. This state varies from 0 to 1, over time, in an S-shaped manner (Supp. File 1, eq. S12) with 1 representing a fully mature colony wherein the queen is completely emancipated from any colony tasks beyond reproduction.

Next, we recognize that colony maturation rate is not a constant as suggested above. Since, as noted earlier, pathogens most readily impact young instars (i.e., immature individuals), we assume that colony-wide infections reduce the rate of colony maturation due to a lack of immatures recruiting into terminal castes (Supp. File 1, eq. S13). In other words, higher rates of infection lead to lower maturation rates making colonies even more susceptible.

Further, we assume that colony-wide immunocompetence is determined by the maturation state because the former maps directly onto colony maturity by the function which is species-specific. Thus, maturation rate is a function of estimated pathogen risk and maturation state (Supp. File 1, eq. S14).

Similarly, highly virulent pathogens can threaten the life of the entire colony but the degree to which they do so will also depend upon colony-wide immunocompetence as described earlier (Supp. File 1, eq. S15). If the queen invests in TGIP during period t, fewer progeny are produced that might otherwise recruit into terminal workers, soldiers and alates, as such, the maturation constant r is reduced. Taken together, maturation rate r is no longer a constant but rather a function of pathogen risk, information state, colony maturation state and investment into TGIP (Supp. File 1, eq. S16).

Fitness to the colony from alate production can be described by a function that includes the risk of infection to the colony. Since immatures are the instars most susceptible to infection, we assume that disease reduces recruitment of immatures into older castes and alates. Thus, we replace the discounted fitness function $\eta(c,\tau)\mu_{\xi}^{a}$ from our original model with:

$$\eta(M,\tau)\mu_{\xi}^{a}\mu_{\gamma i}^{'}(Q,\tau)$$

where: fitness from alate production is discounted by non-pathogenic and pathogenic events with the latter modified by probability that such an event will occur, further modified by colony-wide immunocompetence and TGIP.

Taken together, the modifications can be implemented in a dynamic state variable model as follows:

$$F(\rho,M,Q,t,T)=\max\tau\ \eta(M,\tau)\mu_{\xi}^{a}\mu_{\gamma i}^{'}+\mu_{w}\mu_{\gamma i}^{'}\left[\begin{array}{c}(1-\gamma_i)F\left(\rho',c',\psi',\chi',Q',t+1,T\right)+\\ \gamma_i\left(\rho',M',Q'',t+1,T\right)\end{array}\right] \quad (4)$$

The model can be read from left to right as in Eq. 2, however, note that colony infection and immune states are not included as dynamic states as part of our model simplification process. Thus, we read as: the expected fitness for a colony with wood resources ρ, maturation state M and knowledge state Q at time t with a maximum lifespan of T is equal to: fitness from production of alates (discounted by the product of survival rate and the time it takes to become an alate), η, as a function of colony composition and size and investment in TGIP, plus future production discounted by the probability invasion by the focal pathogen and non-pathogen threats. This expected future production depends upon whether the queen perceives presence of the focal pathogen. If so, no pathogen is perceived with probability $\prod_{i=1}^{P}(1-\gamma_i)$ and discounted by the probability of surviving into the future given non-pathogen mortality factors (e.g., floods) μ, the colony can expect future production of alates, dependent upon the updated state variables, in particular, expected increased risk regarding pathogens. At least one pathogen is perceived with probability $1-\prod_{i=1}^{P}(1-\gamma_i)$.

Discussion

Our current theory for adaptive TGIP in termites is another take on the classic offspring quantity-quality tradeoff that cuts across most living organisms (Stearns 1992). What makes this particular slant nearly unique is the social context. The marginal returns from investing in offspring quality depend greatly on the social milieu and ecological circumstances, in particular, the risk from pathogens, which can vary significantly in time and space.

Here, we have taken two approaches, within the same dynamic framework, to model adaptive TGIP. In both cases, we attempted to include many key basic and empirically tested socio-eco-immunological aspects of termites (Rosengaus et al. 2011a; Cole et al. 2018; Cole and Rosengaus 2019, 2020a, 2020b). As such, we consider both models as effectively emulating the natural dynamics among the three key life-history traits when eusocial individuals experience pathogenic stress (Fig. 1). The question remains as to whether our simplified model could generate the same predictions as the more nuanced detail-rich one, but in a more general way. Given the interplay between dynamic states, we expect that both models will have non-obvious emergent properties though not necessarily the same ones. If so, would relaxing some of the assumptions from the detail-rich model produce generalities that will now allow us to make predictions for a broad range of social organisms including subsocial species?

Earlier we argued that employment of the dynamic state variable approach to studying adaptive TGIP would yield unique insights that would not be obvious otherwise. While it is beyond the scope of this paper to engage in detailed analyses of our models, inspection of the dynamic models (Eq. 1, 2, 4) generates some novel insights and predictions. Below, we discuss this inspection, state by state. In addition, we provide a further set of predictions of particular attributes of termite TGIP (Supp. File 3).

Resource state: *Zootermopsis,* and likely most other termite species, lives under significant resource constraints. The wood exploited by *Zootermopsis* is extremely variable in quantity and quality. Yet, eventually, such nesting and feeding resources are finite (Abe 1987). The size of the log (wood quantity), the wood species and its degree of decomposition (wood quality) likely influence colony growth rates, caste composition, colony demography (Lenz 1994) and ultimately, colony survival and overall fitness. Moreover, the termites' cellulose-based diets are nitrogen

poor (Shellman-Reeve 1990, 1994; Nalepa 1994). Because nitrogen is an integral building block of antimicrobial peptides, important in gametogenesis (for example vitellogenins; Cole et al. 2020b) and required for somatic growth at both the individual and colony levels, this nutritional limited resource is bound to foster trade-offs among different life-history traits, including immunocompetence, parental investment and the colony's social structure. The long-term consequences of such trade-offs within the parental colony can affect the quantity and quality of the fertile dispersing caste, the alates (future queens and kings). Depending on the colony of origin, *Zootermopsis* alates are known to vary significantly in their size and mass (Cole et al. 2018; Cole and Rosengaus 2019). Mass in particular, can be used as a proxy of resource acquisition (Berger et al. 2012; McConnel and Judge 2018) and recent work has demonstrated that *Zootermopsis* alate mass significantly influences their probability of colony establishment after swarming (Cole et al. 2018; Cole and Rosengaus 2019). From the queen's perspective, her mass is a significant predictor of both the likelihood and onset of oviposition. Interestingly, the presence of heavy king as a mating partner also significantly influences her survival, her onset of oviposition, overall egg production, and hatching success (Cole and Rosengaus 2019). These interesting results and the fact that kings and queens engage in biparental care during colony foundation (Rosengaus and Traniello 1991) suggests that well-resourced kings are better at assisting their mate during their crucial initial stages of colony foundation, a time when the queen faces multiple competing and energetically costly demands such as copularium construction, mating, oogenesis, oviposition and egg care; Cole et al. 2018). It should not be surprising that if alates have to cope with imminent pathogenic threats during colony foundation in addition to all these other demands, then the probability of establishing a new colony should be low. This is indeed what we have reported in the past: ~ 40–60% colony failure at 1 month post-pairing; Rosengaus and Traniello 1993a; Cole et al. 2018). All of the above reinforces the need to include the resource state in TGIP theory as it is reasonable to assume that queens and kings on poor resources will be less likely to express TGIP simply because of the high relative cost of doing so; Fig. 1d). We also expect TGIP to be rarely expressed in colonies that are near extinction wherein wood resource are nearly spent, not because the physiological cost is too high but rather because the return on investing in the future via TGIP will not be reaped; this is akin to end-of-life predictions for solitary organisms (Roitberg et al. 1993). Finally, although our theory was developed with one-piece termites in mind, we can apply our models to termites (or other social organisms) that forage outside the nest by adding yet another decision variable regarding how much they forage, which then would impact TGIP decisions particularly from the perspective of colony state (see immediately below).

Colony state—based on past empirical results, young colonies are extremely susceptible to infection and failure (Rosengaus and Traniello 1993a, b; Hartke and Rosengaus 2013; Cole et al. 2018; Cole and Rosengaus 2019), and their ontogeny is impacted by pathogens via reduction of progeny and delayed developmental milestones (Calleri et al. 2006; Cole et al. 2018). These in turn likely slowed-down transition rates from one instar to the next, one caste to another, potentially retarding queen emancipation. This leads to the novel prediction that all else being equal, queens should be more willing to invest in TGIP than one might expect based on a simple quantity/quality trade-off analysis of a state-free model (Stearns 1992). Note the non-obvious and counter-intuitive point that pathogens may have more negative impacts on colony fitness by affecting the colony's social structure (age and caste composition) and its concomitant maturation time than by removing individuals due to death from disease alone.

Infection state—it goes without saying that a colony that is infected with a pathogen will gain more from TGIP than a healthy one (Fig. 1) however, the degree to which this is true will depend upon at least two key factors: who in the colony is infected and how the maturation state of the colony is altered due to the presence of a pathogen. Loss of workers to infection may dramatically reduce colony growth rates and consequently, delay not only queen emancipation but also the timing needed to attain maturity (i.e., the time elapsed between colony foundation and the production of the first dispersing alates). High infection rates in young colonies could place a colony at peril given the lack of workers to mitigate such infections. As such, the marginal gains from TGIP loom large for immature colonies even if there is reduction in queen's fecundity due to high trade-offs (Fig. 1c, d).

Immune state: Our dynamic models (Eq. 1, 2, 4) allow us to hypothesize that if a colony has high baseline immunity and/or high caste/age diversity, then these factors would disfavor the expression of TGIP because of the resulting small marginal gains. Since high caste/age diversity is inherent in mature colonies, emancipated queens would gain little from expressing TGIP under these conditions. Thus, a corollary from the colony state prediction of widespread TGIP (as described above) is that TGIP should only be expressed when baseline immunity and/or colony social structure is low so long as TGIP costs are not exorbitant (Fig. 1c).

Knowledge state—adaptive TGIP plasticity should be conditional on the threat of pathogens being known to the queen and king. In *Zootermopsis* this is not an issue as the queen and king move throughout the nest galleries and therefore could monitor pathogenic risk directly. However, in other termite species where the royal pair is sequestered into the royal chamber away from the colony (i.e., fungus-growing termites), then access to pathogenic threat information

by the reproductive pair may be limited, obtained only indirectly via the workers. Such information transfer would be subject to the frequency with which the royal pair socially interacts with their worker force (akin to false negatives from human pathogen tests) and could potentially arise through chemical or tactile social interactions with their worker force in a fashion similar to the informational exchange when the royal chamber (built around the reproductives) is being constructed by the workers (Camazine et al. 2001). Under these conditions, we would expect expression of TGIP by the reproductive pair to act more in a manner predicted by static, state-free TGIP models in a constitutive fashion (i.e., expression of TGIP should depend on average (global) values of risk).

Time-scale—One of the key challenges we faced in developing our theory was incorporation of different time scales. Long-lived organisms and/or super-organisms might sometimes face challenges that take place over unpredictable, short periods of time and, though rare, might be critical to lifetime organism success. Hastings (2010) noted that transient short-term dynamics may vary dramatically from long-term systems (read here: colony) dynamics, particularly in the structured populations epitomized by social insects. Mangel and Roitberg (1992) showed how adaptive short-term changes in behavior by parasitoid females (read here: termite queens) might generate dynamics that vary from limit cycles to dynamics with strange attractors (Hastings et al. 1993). Thus, a big challenge in future research related to the effects of TGIP on insect populations and their evolutionary dynamics will be to determine appropriate time-scale and, as such, appropriate level of detail. In both of our models, we incorporated biologically realistic short time periods with future discounting (i.e., the ultimate value from producing an offspring is discounted by the probability that it will live to become a reproductive sometime in the future) that allowed us to consider both short- and long-time horizons. This comes at the cost of iterating over many of such time periods though computationally this is not difficult for modern computers.

Degree of sociality—We developed our adaptive TGIP theory with a particular eusocial organism in mind, the one-piece *Zootermopsis* termite species. This unique biology is emphasized in our detailed, nuanced model (Eq. 1, 2) but much less so in our simplified model (Eq. 4). Could our simplified model be applied to a semi-social or solitary organism, say a leaf-cutter bee, and how so? For a leaf-cutter bee, there is no longer linkage between colony state and offspring survival, thus simplifying the model even further. This reduces the problem to an offspring quantity-quality issue however, analogous to our simplified model (Eq. 4) where the mother bee's expectation of life (t relative to T; Eq. 4) and the cost of TGIP relative to offspring performance are critical. In fact, we have demonstrated that alfalfa leaf-cutter bees (*Megachile rotundata*) will vary in their willingness to defend offspring (eggs) against predators and parasitoids in a state dependent manner where the key states are nest value (i.e., offspring number), nest susceptibility and knowledge of predators wherein we manipulated risk from potential nest usurpers (Peterson et al. 2016). Whether they make similar flexible decisions with regard to risk from pathogens remains to be seen but they clearly have the ability to weigh offspring defense trade-offs in a contextual manner as we have postulated for termites.

Lessons learned: context matters

It is understood that our dynamic state-variable approach generates insights/predictions that are more complex and more nuanced than static approaches but this is to be expected.

Applying context to ecological phenomena necessarily increases complexity just because of the addition of conditional dimensions. Notice that all of the predictions above can be derived from our simplified model (Eq. 4). It is not the implementation of great detail (see Eq. 1, 2) that provides context but rather the implementation of biologically appropriate states, whether complex or simple, that matters. Finally, it is easy to see that the insights above could be applied to a range of organisms that sit on the sociality spectrum; state dependence is appropriate for many colonial animals (e.g., Wright et al. 2012).

So where do we go from here? We developed a novel, state-dependent theory for TGIP for eusocial insects. There are several directions we might move from here, including: (i) formal analysis of our theory via backwards induction of equations Eq. 1, 2 and 4 via computer models (Clark and Mangel 2006). Doing so would illuminate critical points or set of conditions where TGIP expression would be favored/disfavored. For example, as suggested but not quantified in our conceptual Venn diagram model (Fig. 1), the adaptive TGIP region should shrink inversely with TGIP production costs—results from backwards induction would determine the exact shape and size of adaptive TGIP region under different conditions; (ii) similar formal analyses of the two models would tell us whether inclusion of detailed infection dynamics is necessary to determine the adaptive TGIP regions or whether simplifying such dynamics as we did with our lean model gives the same quantitative insights; (iii) backwards induction is also valuable in that it generates optimal decision matrices that include best TGIP decisions for all possible combinations of states. Once such matrices are generated, it is possible to include them in computer simulations (i.e., forward induction) for colonies under different ecological situations (Clark and Mangel 2006). From there, we would generate infection epidemiology (e.g., size, frequency and impact) for various pathogens that could be compared with

those found in nature as a means of corroborating our findings; (iv) we propose to employ different types of TGIP in our models (e.g., prefabricated immune-related proteins, transfer of immune-elicitors and epigenetic markers) to see what impacts they have on TGIP decisions and outcomes. The various alternative TGIPs differ in their costs, breadth and persistence. For example, prefabricated immune-related proteins are likely the most expensive, enhance the broadest immune response and are the shortest lasting. As such, the parental contribution of prefabricated immune-related proteins to the progeny should not be the optimal under all circumstances (see predictions in Supp. File 3). In addition, because these different aforementioned types of TGIP might operate at different timescales, their impact on transient dynamics could vary dramatically; (v) we assumed that the pathogens in our models are static and do not evolve in response to termite tactics—a next version of our theory may take the form of a dynamic game between host and pathogens (e.g., Wolf and Mangel 2007); (vi) in building our models, we considered a number of variables for which little empirical information is currently available (e.g., interaction between different pathogens, queen's ability to recognize pathogens, quantitative determinants of colony-wide immunocompetence, etc.). We see theory development and model building working hand-in-hand with experimental and empirical work. Good theory generates good new questions for empirical scientists and good empirical science grounds good theory.

Concluding remarks

Our approach has identified interesting novel questions that merit empirical and theoretical testing in the future. For example, does investment in TGIP vary as a function of the degree of colony maturation, colony social structure (including age and caste composition), and the degree of social interactions amongst all colony members? Is TGIP fixed or plastic, and does it vary in a context dependent fashion? Are the inevitable trade-offs between different life-history traits dictating the levels of expression of TGIP? When should TGIP be deployed? Does the nature of TGIP (i.e., transfer of prefabricated functional effectors, immune-elicitors and/or epigenetic markers) influence the amount of time progeny is protected? Is TGIP replaced by colony-wide immunocompetence as the colony matures? Do the nesting, feeding and foraging ecologies of different species modulate TGIP? Does the nature and duration of TGIP differ between hemimetabolous and holometabolous eusocial insects? Answers to these and future questions will likely propel the field forward in interesting directions. We invite and encourage our fellow scientists to consider addressing these possible questions.

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Author contribution BDR and RBR contributed equally to this work. Both conceived the research question, both wrote the ms and reviewed/approved the final product. BDR generated the model equations based on the biological context which was provided by RBR.

Data availability Data sharing is not applicable to this article as no datasets were generated or analyzed.

Declarations

Ethics approval n/a.

Consent to participate n/a.

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