Adaptive suicide: is a kin-selected driver of fatal behaviours likely?

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Abstract

While several manipulated host behaviours are accepted as extended phenotypes of parasites, there remains debate over whether other altered behaviours in hosts following parasitic invasion represent cases of parasite manipulation, host defence or the pathology of infection. One particularly controversial subject is “suicidal behaviour” in infected hosts. The host-suicide hypothesis proposes that host death benefits hosts doomed to reduced direct fitness by protecting kin from parasitism and therefore increasing inclusive fitness. However, adaptive suicide has been difficult to demonstrate conclusively as a host adaptation in studies on social or clonal insects, for whom high relatedness should enable greater inclusive fitness benefits. Following discussion of empirical and theoretical works from a behavioural ecology perspective, this review finds that the most persuasive evidence for selection of adaptive suicide comes from bacteria. Despite a focus on parasites, driven by the existing literature, the potential for the evolution of adaptive suicidal behaviour in hosts is also considered to apply to cases of infection by pathogens, provided that the disease has a severe effect on direct fitness and that suicidal behaviour can affect pathogen transmission dynamics. Suggestions are made for future research and a broadening of the possible implications for coevolution between parasites and hosts.

Keywords

Adaptive suicide – Behavioural ecology – Evolution - Host suicide hypothesis – Inclusive fitness - Parasitism

Introduction

Across all taxa that are involved in parasite-host relationships, a range of exploitative and defensive mechanisms have co-evolved in the respective 'sides'. A key question is whether some of the behaviours displayed by parasitized animals represent adaptations of the host or their parasite [1]. Behavioural changes following parasitic invasion vary greatly in their magnitude [2]; and the adaptive significance, if any, is not always clear. One possibility is that altered behaviours may simply be a response to the pathological effects of parasites, and are not necessarily adaptive to either parasite or host. However, Moore [3] warns against explaining altered behaviours as 'side effects' of 'pathology', arguing that the fitness outcomes for participants in host-parasite associations, including parasite-induced behavioural alterations, will be subject to natural selection and therefore we should expect them to be more likely than not explicitly linked with the evolution of those species involved. Mostly though, studies focus on attributing behaviours to parasite adaptation or host adaptation.

On the one hand, if altered host behaviours are adaptive for parasites, they should facilitate the completion of their lifecycle. This is typically achieved either by diverting the host's energy away from their own reproduction to the parasite for growth [3-6] or by rendering intermediate hosts more vulnerable to ingestion by the parasite's definitive host [3, 7-10]. Where the life cycle of parasites involves stages that spend some time in a particular external environment, host behaviour can also be manipulated for the successful dispersal of parasite propagules in their most suitable conditions [1, 3, 11-13]. Interestingly, Poulin et al. [14] suggest that hosts may be capable of opposing some behavioural manipulation by established parasites, but the idea has received little attention. Certain host responses to infection by helminth parasites suggest that some hosts can remain at least partially in charge of their body, but lack of data is unsurprising because where infected hosts behave normally opposition to manipulation would not be differentiable from a parasite's failure to manipulate [14].

On the other hand, hosts may benefit from behavioural changes following parasitism. Most obviously, behaviours that serve to minimise damage from an internal parasite may reduce the negative impact of parasitism on a host; such as exhibiting sickness behaviour [15], behavioural fever [16, 17] or self-medicating foraging [18, 19]. More intriguingly, a host individual may benefit by sacrificing its direct fitness for the sake of increasing its inclusive fitness [20, 21]. One fascinating, but controversial, mechanism through which this could occur is so-called "adaptive suicide" behaviours where post-invasion behaviours function to eliminate the propagation of an established parasite thus protecting kin [22, 23].

Adaptive suicide

The host suicide hypothesis [22] proposes that a host may use its own death to increase its inclusive fitness [20, 21]. Where a parasitic infection effectively causes sterility or death, the host will be unable to improve its own reproductive fitness; suicidal behaviour could enhance its inclusive fitness by preventing the maturation of its parasite and lowering the risk of parasite infection for relatives [22]. The fitness cost associated with death becomes negligible when a host's own expected reproduction approaches zero [23]. Provided that the host's death (and that of its parasite) reduces the level of subsequent parasitism in its kin relative to that in non-kin, there should be a positive selection value on the behaviour. Smith Trail [22] argued that natural selection should drive the evolution of suicidal behaviour even when increases in inclusive fitness are very small, provided that: 1) the host's individual fitness is zero, 2) that upon emergence from the host parasitoids are more likely to infect the host's kin than non-kin, and 3) the kin's reproductive success is increased due to the subsequent lowered risk of parasitism.

In order to satisfy these requirements, adaptive suicide was predicted to be most prevalent in colonial or social host species, or in members of host populations with low dispersal rates and a relatively high degree of inbreeding [22]. Conversely, parasitoid species with relatively small search ranges or areas

of discovery would be particularly vulnerable if their hosts adopted this behaviour [22]. Suicidal behaviour can include activity that makes the individual more conspicuous to predators or easy to capture [22], or causes great costs in terms of energy spent, lost feeding opportunities and probability of death [23].

Empirical work

Aggregating insects: Aphids

McAllister and Roitberg [23] reported what they believed to be the first convincing evidence in support of Smith Trail's [22] host suicide hypothesis, following their observations of pea aphids (*Acyrthosiphon pisum*) from different regions parasitized by the braconid wasp *Aphidius ervi* apparently exhibiting suicidal behaviour to different extents. Both in response to aphid alarm pheromone and approaching coccinellid predators, aphids for whom the risk of death due to heat stress and desiccation was thought to be higher dropped more frequently when parasitized whereas aphids from cooler coastal regions behaved no differently when parasitized to when unparasitized [23]. From this, McAllister and Roitberg concluded that in a habitat where alternative escape tactics result in significant differences in mortality risk (interior regions), parasitized aphids chose the riskiest behaviour. Meanwhile in the habitat where alternative escape tactics result in no apparent difference in mortality risk (coastal regions), parasitized aphids behaved no differently to unparasitized aphids. Curiously, though, in both situations, parasitized aphids did not drop from plants without mediation by predation [23]. This study received a number of criticisms from Latta [24] and Tomlinson [25] which McAllister and Roitberg [26] addressed as "misunderstandings" in a rebuttal, but the fact that adaptive suicide in this system was predator-mediated arguably suggests that the adaptation concerns more the survival of the parasitoid rather than a benefit to the aphid. If this is not the case, it makes little sense why aphids should not allow themselves to be consumed by predators. Indeed, we find in some more recent cases - discussed in greater detail later – that increasing mobility following invasion by a parasite may increase an aphid's likelihood of being consumed by a predator [27-29].

McAllister and Roitberg went on to examine adaptive suicide in parasitized pea aphids of varying reproductive potential [30]. When aphids are parasitized at the second instar stage, they have no reproductive future and will not produce any offspring prior to mummification. However, aphids parasitized in their fourth instar can expect to produce seven to eight offspring before dying, directly increasing their own fitness, and so the cost of any altruistic behaviours upon parasite invasion may increase relative to the payoff for these individuals. Aphids parasitized at the second instar were found to utilise dangerous escape behaviour (dropping) when approached by a predator, while aphids parasitized at their fourth instar behaved no differently from unparasitized individuals [30]. This result was consistent with their prediction that as the cost of altruistic behaviour increases relative to inclusive fitness payoff suicidal behaviour should disappear, however the escape behaviours were again elicited by the presence of a predator, weakening any support for a host-benefitting adaptation [30].

Many aphid species disperse away from their colony mates and mummify elsewhere following parasitism, but there is not always evidence to suggest that this behaviour is host- or parasitoid-mediated [31, 32]. It is also possible that both parasitoid and host benefit to an extent. Perhaps the host gains indirect fitness benefits by transporting the parasitoid away from kin, while the parasite does not suffer from this so long as it is no more challenging to find some (non-kin) aphids.; Moreover, the parasitoid might actually benefit if the move is to a safer microclimate [33]. Considering other potential evidence for altruism in non-eusocial parthenogenetically reproducing aphids, Wu and Boivin [34] looked at the smearing of cornicle secretions by cereal aphids (*Sitobion avenae*) onto parasitoids (*Aphidius rhopalosiphi*). Cornicle secretions of aphids were concluded to be altruistic against parasitoids, as they provided no direct fitness benefits to secretion-releasing individuals, only indirect fitness benefits through negatively impacting the parasitoid's subsequent foraging time and offering some protection to neighbouring clone-mates [34]. Smearing also occurred more frequently

when a greater number of clone-mates were present, increasing inclusive fitness benefits [34]. This appears to be a case of kin-directed altruistic defence outside eusocial animals. Interestingly, non-social aphids also appear to possess surprising kin-recognition abilities, varying in aggregation and defensive abilities depending on the relative presence of clonemates and non-kin [35].

With an increased awareness of the potential for aphids to recognise kin, it is interesting to consider that adaptive suicide following parasitism in the presence of predators need not involve dropping from, or leaving, an area to altruistically remove a parasite. Meisner et al. [27] demonstrated that pea aphids at earlier stages of parasitism suffer higher predation by the coccinellid predator *Harmonia axyridis* than unparasitized aphids. Duran Prieto et al. [28] proposed that if the behaviour of parasitized aphids was the cause of their more intense predation, it should be expected that parasitized aphids will suffer greater predation from predators other than coccinellids, especially if their behaviour has an adaptive value. They explored predation of recently-parasitized pea aphids by the hemipteran *Macrolophus pygmaeus*, obtaining a similar result to Meisner et al. [27]. As the predation rate was not affected by the ratio of parasitized to unparasitized aphids, the energy and nutrition obtained from both prey types can be assumed to be equal and therefore prey preference was likely down to aphid behaviour rather than physiology. Higher mobility after being parasitised was evident. It is therefore plausible that the suicidal behaviour seen in pea aphids following parasitism [23, 30], can function by increasing the rate of encounter between the predator and the parasitized prey [28]. By behaviourally offering themselves up, as well as removing the parasite from the area parasitized hosts may help satiate predators in order to protect unparasitized kin. This hypothesis is supported by the observation of Meyhofer and Klug [29] that a lacewing predator *Chrysoperla carnea* took significantly less time to capture a parasitized black bean aphid (*Aphis fabae*) as its next victim than an unparasitized one.

Eusocial insects: Bees and ants

Schmid-Hempel and Müller [36] reported that worker *Bombus lucorum* bumblebees parasitized by conopid flies remain outside the nest longer than unparasitized workers during foraging hours and may abandon the nest altogether. They suggested that this would benefit the parasitoid pupae as they might be less subject to the infections that can develop on abandoned combs in bumblebee colonies. However, Poulin [37] suggested that these changes in behaviour are more plausibly an adaptive response of the host resulting in inclusive fitness and therefore an example of the adaptive host suicide as proposed by Smith Trail [22]. Fritz [38] pointed out that natural selection should favour parasitoids that manipulate the host in ways that reduce its mortality likelihood before the parasitoid pupates, but bumblebees would in fact be more susceptible to predation, starvation and superparasitism outside the nest [37].

However, the conopid-bumblebee association does not meet the conditions of adaptive host suicide as laid out by Smith Trail [22] for two reasons: 1) by the time adult conopids emerge from pupae, the host's kin have dispersed or died; 2) adult conopid females spread widely away from their site of emergence and so would not preferentially infect the bumblebee's kin even if the bumblebee allowed it to live [37]. McAllister and Roitberg [30], though, pointed out that early death of a parasitized host will be adaptive as long as the costs of decreased reproductive success are outweighed by the benefits of increased inclusive fitness. Poulin [37] argued that the costs of death for a parasitized bumblebee worker is in fact very low as its reproductive potential approximates zero following infection, as does its use as a forager in the colony. On the other hand, leaving the nest could increase a bee's inclusive fitness as parasitized workers are susceptible to further attack from conopid flies, and so leaving the colony may attract fly attacks away from non-parasitised kin [37]. Additionally, by leaving a nest, a parasitized bee with lower foraging efficiency might avoid depleting the colony's food stores for its own, unproductive survival, thus leaving more available for its kin [37] – a behaviour we here dub the "Captain Oates Effect".

Poulin's [37] interpretation, though, was criticised in response by Müller and Schmid-Hempel [39]. Bumblebees tend to intermingle with foragers from many different colonies when outside their nests, staying outside the colony and acting as a target for fly attacks is very likely to protect kin and non-kin from parasitisim to similar degrees; the benefits would not be disproportionately routed towards kin to the extent that the kin-selection hypothesis requires [39]. Müller and Schmid-Hempel [39] also argued that, from their observations, there is no evidence that parasitized bumblebees are not able to feed for themselves on flowers and so they would not necessarily depend on food stores in the hive anyway. Müller and Schmid-Hempel [40] subsequently found evidence of parasitized bumblebees exploiting cold temperatures as a defence against parasitoids. Parasitised workers stayed in the field overnight instead of their nest, where the cold temperatures could retard the maturation of the parasite, reducing its chance of successful development. In choice experiments, parasitized bees were also demonstrated to actively seek out cold temperatures [40]; although not supportive of adaptive suicide, these findings did suggest a larger role for host advantage rather than pure parasite manipulation.

Unrelated to parasitism, apparently altruistic self-removal from the hive has been reported in health-compromised honey bees (*Apis mellifera*), whose presence may be harmful to their colony [41]. Other studies have previously suggested that different eusocial insects permanently leave their colonies when infected [42, 43], but it is difficult to pick apart host adaptation from potential parasitic manipulation, or indeed pathological trauma. Through artificially compromising honey bee foragers, Rueppell et al. [41] provided experimental evidence that self-removal need not be caused directly by parasitic manipulation or related to stress-induced foraging [44] or loss of orientation abilities [43]; altruistic self-removal could be a host adaptation to increase inclusive fitness. Further, a simple model suggested that altruistic self-removal by sick social insect workers, in order to prevent disease transmission to kin, is expected under most biologically plausible conditions [41]. When occurring

206 after infection from a parasite, self-removal from a colony might in some cases qualify as adaptive
207 suicide.
208
209 However, colony desertion following parasitism certainly does not always come from altruism. Hughes
210 et al. [45] describe a fascinating behavioural change in the paper wasp *Polistes dominulus* following
211 infection by the strepsipteran parasite *Xenos vesparum* which culminates in colony desertion and the
212 formation of extranidal groups in which up to 95% of occupants are parasitized females. While
213 altruistic desertion to reduce infection of kin would generally be a good strategy for infected social
214 insects, this is untenable in this case because female *X. vesparum* parasites are only infective if
215 inseminated and wasp copulation does not occur on the nest due to occupants vigorously attacking
216 free-living males. The nest desertion and aggregation by infected wasps is most likely a case of
217 adaptive parasite manipulation of host behaviour in order to facilitate parasite mating [45].
218
219 As in aphids [27-29], however, adaptive suicide in eusocial insects may not always involve spatial
220 separation of a host from its kin; selective predation on parasitized hosts could also help hosts
221 altruistically protect their unparasitized kin from a parasitoid. Mathis and Tsutsui [46] studied the rove
222 beetle *Myrmedonota xipe*, which associates with – typically highly aggressive – *Azteca sericeasur* ants.
223 Rove beetles were found to selectively locate and prey upon ants parasitized by phorid parasitoid flies.
224 Parasitised ants acted less aggressively towards the beetles than healthy ants, meaning that rove
225 beetles can eat them alive without interruption [46]. Unable to access the aggressive, unparasitized
226 ants as a food resource, *M. xipe* appeared to almost exclusively prey on parasitized ants, but this could
227 also benefit the infected ants as being consumed would reduce the phorid fly population free to infect
228 their kin. On the one hand, this system seems a good candidate to meet the criteria for the host-
229 suicide hypothesis as *A. sericeasur* is a polygynous and polydomous social insect that forms wide-
230 spanning territories and so emerging mature parasitoids are far more likely to encounter their host's
231 kin than non-kin [46]. On the other hand, it may be that not all phorid fly larvae successfully mature,

and so selective predation of ants that would survive parasitism would ultimately cost the colony as a whole [46]. Parasitised workers may also be active colony members during the development of the parasitoid, and in these cases the benefit of eliminating the larvae via predation may be offset by the costs to the colony incurred from losing productive parasitised workers [46]. Further work exploring the true costs and benefits of selective rove beetle predation to parasitized ants will certainly shed more light on the evolution of this system but, as Mathis and Tsutsui conclude, beetle predation may indirectly benefit ants where parasitized ants can reduce the numbers of developing parasitoids by increasing their appeal as prey. Selective predation on parasitized hosts, beyond aphids, has been demonstrated in several studies, including in lepidopterans [47] and non-eusocial hymenopterans [48] (also see review by Rosenheim et al. [49]); exploring the possibility of this as a pre-emptive adaptive suicide strategy across different taxa will also be useful in advancing understanding of responses to parasitism.

Bacteria

An extreme defensive immune strategy in bacteria against phages is the deployment of abortive infection (Abi) systems that abort phage infection but also lead to the death of the infected bacterial cell [50]. Abi systems protect neighbouring bacteria at the expense of the individual expressing the trait [51]. Altruistic deployment of Abi systems is particularly likely to be selected for where a bacterium's neighbouring cells are kin emerging from clonal expansion or, additionally or alternatively, cells have other factors that favour cooperation, such as aggregation as part of a biofilm [52, 53]. Makarova et al. [52] hypothesised that immunity and suicide systems in bacteria are coupled and that complex decision-making involving sensing the course of a viral infection may determine whether the response to a virus involves induction of dormancy, an immune response, or suicide in the face of immune system failure. Works investigating recently discovered Class 2 CRISPR-Cas (Clustered Regularly Interspaced Palindromic Repeats and CRISPR-associated genes) systems [54-56] have since found the most direct link between immunity and programmed cell death in microbes discovered yet

[57]. It is thought that immunity-suicide coupling is favoured in situations where a system includes dual function components that are involved both in immune and in suicidal activities [58]; this could be the case for some Cas proteins [57].

The 'decision' to commit adaptive suicide in bacteria likely involves diverse signal transduction pathways [52]. In eukaryote yeast cells (*Saccharomyces cerevisiae*), natural programmed cell death is thought to hinge on the degree of damage to genetic material, with its critical value determined by quorum-sensing machinery [59]. Quorum-sensing is also an important process in prokaryote bacteria cell-cell communication, wherein extracellular signalling molecules are produced, detected and responded to [60, 61]. Quorum sensing has been found to be important in the sporulation-competence decision in *Bacillus subtilis* [62, 63], and Hazan et al. [64] recently described a novel quorum-sensing-regulated bacterial mechanism that controls self-poisoning of the respiratory chain in *Pseudomonas aeruginosa*, providing a fitness benefit to the microbial collective. A mechanism involving quorum-sensing is likely to be an important element in the mechanics of adaptive cell death following infection in bacteria [52].

Beyond sensing population levels by quorum-sensing, proteins that can sense damage and 'predict' the outcome of infections will also be important in mediating Abi systems and toxin-antitoxins [65, 66] that colocalise with immunity genes [57]. The exact mechanisms and structures that forecast the course of virus infections remain to be fully elucidated, but it is thought that whenever dedicated sensor molecules indicate an attack is manageable the cell mobilises its immune system, while if the indications of attack are dire then self-afflicting programs are triggered [57]. Switching from the immune mode to the suicidal mode of defence may be in part governed by sensors determining the level of damage inflicted on a cell [57]. Intriguingly, though, type VI-A CRISPR-Cas systems appear to take a short-cut in the cell's usual response relay by simplifying – or even skipping – the damage-sensing step and employing the main immune effector as the suicide effector as well, but these

284 systems are rare in bacteria perhaps suggesting that foregoing damage-sensing is costly [57].
285 Predictive and damage-sensing signals read and responded to by various sensors likely differ between
286 defence systems (see [57] and references therein for details).
287
288 Several studies suggest that spatial structure and migration are important to the evolution of bacterial
289 suicide upon infection as they impact relatedness and therefore the relative benefits of kin selection
290 [67-71]. For example, Fukuyo et al. [69] competed altruistic *Escherichia coli* with an artificially
291 engineered suicide mechanism against wild-type bacteria in the presence or absence of the phage λ.
292 They found that in a spatially structured soft agar environment, altruistic suicide had a selective
293 benefit for the bacteria, but this was not the case in a well-mixed liquid environment. Using the
294 naturally-occurring Abi mechanism 'Lit' in *E. coli*, Berngruber et al. [67] varied the amount of mixing
295 in environments more continuously and found again that spatial structuring was needed for the
296 evolution of altruistic suicide but also that too little mixing might prevent the evolution of abortive
297 infection due to the reduced parasite spread under those conditions. A further study by Refardt et al.
298 [70] confirmed these findings using the best characterised Abi system, 'Rex' in λ-lysogenic *E.coli* strains
299 [50]. Refardt et al. [70] demonstrated that adaptive suicide can evolve even when genetic similarity
300 between neighbouring strains is relatively low in their study of *E. coli* responding to the attack of an
301 obligately lytic phage.
302
303 **Theoretical work and evolutionary predictions**
304 As discussed above, interpretations of empirical data that support the host suicide hypothesis [23, 28,
305 30, 37] have often been criticised [24, 25, 39]. The adaptive significance of host suicide in particular
306 has been challenged because the main supporting studies involved clonal aphids that aggregate [23,
307 30] or eusocial Hymenoptera [36], where complex life histories have made it difficult to exclude
308 alternative explanations or carry out rigorous analysis of fitness [70]. Even in *Euphydras phaeton*
309 caterpillars and their parasitoids – suggested by Smith Trail [22] as an appropriate system for testing

the hypothesis of host suicide – adaptive suicide has not yet been demonstrated to be more plausible than the behavioural changes serving to increase the parasitoid's chance of escaping predation and parasitism itself [72]. Yet theoretical work has convincingly revealed the conditions required for host suicide to evolve [22, 30, 71].

Smith Trail's original hypothesis [22] logically suggested that adaptive suicidal behaviours would increase the inclusive fitness of a parasitized host if the following conditions were met: 1) suicidal behaviour prevents the parasite's maturation and emergence; 2) the mature parasite is more likely to infect the host's kin than non-kin; and 3) the benefit to the host, in terms of the increased fitness of the kin, is greater than the cost of the suicide, measured in terms of the loss of the host's own reproductive fitness. If not all of these conditions are met, early death of the host may still be adaptive as long as the costs of decreased reproductive success are outweighed by the inclusive fitness benefits [30]. One of the key points here is perhaps that the parasite infection must have a severe, if not lethal, consequence for the host's future reproductive success to ensure that swapping direct fitness benefits for kin-selected benefits would result in a net gain for the infected host. Debarre et al. [71] illustrated via modelling how suicide upon infection can be an adaptation, but only in response to extremely harmful parasites and in spatially structured environments.

Shorter and Rueppell [73] suggested that eusocial insects, rather than just aggregated clonal insects, may provide the best test systems for adaptive suicide due to the high relatedness and relative strength of kin selection. While this may prove to be true, empirical work on bacteria appears to lend the greatest support for adaptive suicide so far, even in conditions of relatively low relatedness. Where suicide carries very low cost for committers in structured environments, because infected cells are moribund with no opportunities for further reproduction, apparent altruism can evolve if such an act provides a large benefit to survivors that then avoid extinction [70]. Conversely, in unstructured

environments self-sacrificial suicide would be futile as it would not preferentially protect relatives and so in these situations individual-based resistance is the best tactic for bacteria to combat phages [68].

Selection for adaptive suicide in bacteria will likely be affected by ecological factors too. Refardt and Kümmerli [68] found that in structured environments suicidal host defence was slightly less efficient than individual-based resistance in withstanding phages. They proposed that the putative lower efficiency of abortive infection might be compensated by a lack of pleiotropic costs compared with those usually associated with individual-based resistance mechanisms. Lion and Gandon [74] further suggest that selection for altruistic suicide should be maximised at low host dispersal and at intermediate parasite dispersal, due to their roles in spatial structuring. Horizontal transfer of altruistic suicide Abi systems may also play an important role in their evolutionary success [74]. However, it remains unclear how adaptive suicide can outcompete simpler bacterial defence strategies preventing initial infection [74] and selection for adaptive suicidal behaviours is yet to be convincingly demonstrated in more complex organisms.

If there are instances where suicidal behaviours will be selected for in infected hosts, this raises the question of how adaptive suicide persists evolutionarily if the parasite species would consistently lose out. One of Tomlinson's [25] issues with McAllister and Roitberg's first study concerning adaptive suicide in aphids [23] was that natural selection on parasites would favour the subversion of such suicidal behaviour that benefitted their hosts, and that "in any ensuing 'arms race', asymmetries of selection should favour the parasite." Blower et al. [75] describe a fascinating means by which a bacteriophage counter-evolved to avoid having its replication blocked by an infected cell's premature suicide. Here, they found the bacteriophage evolving sequences that mimicked the cell's antidote to its own toxins, allowing it to continue replicating without being destroyed by its host's defensive system. However, there are in fact some conditions in which selection on a parasite might not be able to override selection for host-benefitting suicidal behaviour. Firstly, if suicidal behaviour is triggered

by a complex set of stimuli then the likelihood that selection for variation in parasite traits could occur just so in order to subvert such a complex behaviour is perhaps very low [26]. Secondly, in situations where the costs of maintaining such strong control over hosts would be high relative to the payoff parasitoids may not be selected to overcome host behaviours. McAllister and Roitberg [26] give the example of parasites with exceptionally high fecundity, for whom the cost of providing each offspring with sufficient neurotoxins to alter the behaviour of every host would be exceedingly high.

It is also worth considering whether host-parasite interactions may have coevolved over time such that suicidal behaviours in hosts may sometimes benefit both the host and their parasite. As mentioned earlier, it seems plausible to us that there may be cases where a parasite is either neutral towards or may benefit from an infected host dropping or otherwise moving away from its kin. So long as it is possible to encounter hosts of some sort, kin or not, after its emergence, the parasitoid does not need to lose out from the host's behaviour, while the host still gains inclusive fitness benefits from protecting its kin. In fact, if the move away from the host's kin also moves the parasitoid offspring to a safer microclimate for maturation and emergence then perhaps both 'sides' of the interaction benefit from the altered behaviours. It is also not much of a stretch to consider that some of the instances where infected hosts make themselves more vulnerable to predation, either through conspicuous behaviour or movement to particular locales, might aid parasites with particular life histories that require transmission from intermediate to definitive host while also sating predators to protect the host's kin. While it would be difficult to parse out whether a host's kin truly benefit from these sorts of scenarios, given that the parasite evidently succeeds in being transmitted to its definitive host, we consider it likely that the benefit of a host's behaviour to either the host or the parasitoid is context-dependent. As an example, nest abandonment by bumblebees could benefit the host more than the parasite in cases where the parasite is highly abundant and virulent and nest cleaning behaviours will be overwhelmed; this is discussed further in the next section. It is important that the full population dynamics at play are considered where possible.

387

388 **In which situations might adaptive suicide evolve?**

389 While the focus of this paper has been on host adaptations following infection by parasites, because
390 previous work in this field has focussed on parasitism, we see no reason why cases of infection by
391 disease should not also lead to the evolution of suicidal behaviours that benefit the hosts. The key
392 aspect to both diseases and parasites that can potentially provoke the evolution of adaptive host-
393 suicide is that they must have a severe effect on direct fitness, otherwise it is unlikely that a
394 behaviour will evolve to compromise direct fitness in order to boost indirect fitness. A major means
395 by which pathogens or parasites can impact direct fitness is by being highly virulent. If virulence is
396 not high, then a behaviour that sacrifices a host's direct fitness to favour enhancing indirect fitness
397 would not evolve. If virulence is high, the evolution of this behaviour is more likely, but the host
398 behaviour must also be able to affect the transmission dynamics of the pathogen or parasite – this
399 rules out some parasites, but also some highly virulent pathogens. It is easy to imagine how the
400 transmission of helminths and the like can be affected by host behaviours, but for biting insects that
401 just collect a blood meal and do not lay their eggs in or on a host, host behaviours will not influence
402 their transmission.

403

404 Considering as an example, then, adaptive suicide should not develop in humans as a response to
405 parasites like tsetse flies because they are not virulent enough. Nor would it develop in response to
406 the protozoa that use the tsetse fly as a vector and cause sleeping sickness [76]. Even though
407 sleeping sickness is highly virulent, killing virtually anyone untreated, the pathogen is spread only
408 when another biting insect takes a blood meal from the infected person [76]. An infected individual
409 could kill themselves as soon as they realised they were infected, thereby reducing their appeal to
410 further tsetse flies as their body cools. However, it is not obvious that this reduction in pathogen
411 prevalence would benefit kin in any meaningful way because the lifecycle of the pathogen in the fly

takes three weeks (from feeding on one person to being able to be spread to another), during which time the tsetse fly will have travelled a long distance; there is little likelihood that the tsetse fly would spread the pathogen from you to your kin.

On the other hand, other taxa may be expected to evolve host suicidal tendencies when infected with particular pathogens and infections, as well as with certain parasites. We have already touched upon earlier cases where ants infected by fungal disease isolate themselves from their colonies [42], but while entomopathogenic fungi may experience increased transmission from their host's dispersal [41, 77] this behavioural manipulation by the disease may be a co-option of host adaptive suicide. While nest hygiene behaviours in ants – e.g. removal of infected individuals or sequestering of individuals within the nest before individuals reach the infective stage – are typically a more effective fitness-enhancing strategy in the face of infections, adaptive suicide could evolve where infection rates are rapid and so extensive that the hygienic response is overwhelmed [78, 79].

Conclusions and suggestions for future research

There is a lack of consensus on adaptive suicide. On the one hand, the behaviour seems theoretically very plausible as a highly effective host adaptation given an extremely harmful parasitized state and fate of significantly reduced direct fitness opportunities. On the other hand, empirical work has so far received much criticism and teasing host adaptation apart from alternative explanations has proven difficult to do definitively. The best evidence, theoretical and empirical, for the selection of adaptive suicide in infected individuals originates in studies of bacteria and Abi systems.

One useful approach for future research – highlighted by Müller and Schmid-Hempel [39] in relation to parasitized bumblebees but true of any study on behavioural alterations upon parasitic invasion – would be for detailed measurements of costs and benefits for both the host and its parasitoid to be

carefully analysed, along with any influence physiological stress may have. Including a consideration of the wider population dynamics and ecological context may be an important component of weighing up the net benefits to host and parasitoid. Elucidating the proximate mechanisms underpinning alterations of host phenotype [80], wherever possible, would also be valuable where they could help identify parasite manipulation – or indeed rule it out in favour of host adaptation or pathology. More behavioural studies on generally self-destructive behaviours in social insects, including cost-benefit analyses and mechanistic studies, are also needed [73] and comparisons between disease-related, condition-related and parasite-related behavioural changes may then shed more light on the potential for adaptive suicide upon infection relative to other explanations.

With regards to non-eusocial species that tend to aggregate with clonemates, Duran Prieto et al. [28] propose a convincing explanation of how suicidal behaviours may lead to increased predation of parasitized aphids. Further studies should seek to investigate whether predation rates on unparasitized kin decrease thanks to parasitized aphids substantially increasing their own personal risk of predation by performing particular behaviours. It would be of great interest whether further studies could prove that, at an early stage of parasitism, greater susceptibility of parasitized aphids to predation is a common phenomenon [28].

From a different perspective, it would be interesting to explore whether there are any host-parasite systems that result in an infected individual decreasing its own fecundity in order to prevent parasites producing infectious units that could then infect its kin. This would perhaps be considered adaptive "reproductive suicide", wherein all future reproduction and direct fitness is cut off, but perhaps where an individual could continue to assist kin without infecting them, thus, it need not dispose of itself entirely. The reduction of host fecundity following parasitic invasion has previously been suggested as an adaptive strategy for damage limitation in some cases [81]. Hurd [82] describes how female host fecundity reduction in the association between metacestodes of the rat tapeworm (*Hymenolepsis*

diminuta) and a beetle intermediate host (*Tenebrio molitor*) can benefit both parasite and host. Here the host's rate of egg production is slower upon infection but this is traded off with a longer life span that might ultimately allow lifetime fecundity to equal or exceed that of uninfected females. The parasite can also gain from this if greater life span increases the probability of the beetle being predated, thus increasing the parasite's transmission [82]. Beyond a merely reduced host fecundity, if there are cases where a host ends its fecundity rather than increasing its mortality, a shutting down of reproductive effort could represent an entirely host-benefitting adaptation that might act to protect its kin from multiplied infectious units. Any exploration into such "reproductive suicide" could give a further perspective on extreme kin-selected adaptations in the face of parasitism.

Modelling work exploring the precise relationship of costs and benefits involved in adaptive suicide in social insects could also be of great use in trying to understand in which situations the evolution of suicidal behaviours as a host adaptation could be more plausible than parasite manipulation and/or pathology. In the case of bacteria, future work developing understanding of how altruistic suicide can outcompete simpler defences that prevent infection in the first place would be hugely valuable [74]. Further details on the nature of the switching signals in immunity-suicide coupling in bacteria, the relevant threshold values, and the determinants of these are all intriguing avenues open for future studies [57]. The longer-term effects of adaptive suicide in bacteria on the complexity [83] and evolution of microbial populations will also be interesting to further explore. Broadening the theoretical framework to include awareness of spatial structuring and the diversity of host and parasite life cycles would allow the production of more informative models, and further empirical studies to validate theoretical predictions regarding selection under different spatial structures could also be hugely valuable [74]. The coevolutionary implications of adaptive suicide by bacteria to avoid population-wide infection in spatially structured environments remains ripe for empirical testing [84]. Greater consideration across taxa of where some behaviours could potentially benefit both host and

its parasite – and explorations of where this may apply to cases of infection by pathogens too – could also yield interesting results.

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Authors' contributions

RKH and GDR contributed equally to the writing of the manuscript.

Data accessibility

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We have no competing interests.

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This work required no ethical approval or informed consent.

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