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Selfish and spiteful behaviour through parasites and pathogens

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ABSTRACT

Questions: Can hosts use their parasites or pathogens to decrease the fitness of their conspecifics? Which conditions support the evolution of such harmful behaviour – expressed as spiteful or selfish behaviour?

Mathematical model: I calculate the selective pressure acting on a mutant expressing harmful behaviour. The direction of selection on this social trait is given by its effect on inclusive fitness. Individuals are haploid and form a population of constant size and structured in an infinite island model with migration. Individuals harm others through their parasites or pathogens.

Key assumptions: (1) An infected host may infect several other susceptible conspecifics simultaneously. (2) A variety of immunity mechanisms enables kin members to be immune to a given parasite or pathogen, a sort of kin recognition.

Conclusions: By using parasites to harm non-kin hosts, the harming host may partially align its interests with those of the parasites, even when there is a fitness cost for this act. The cost is compensated by the fact that the parasite may infect several non-kin hosts within a host generation. That is, by infecting several hosts, the ratio (cost to the actor)/(cost to the recipient) becomes very low, hence facilitating the spread of the harming allele. Immunity-mediated recognition of non-kin hosts or of migrant hosts in subdivided populations further helps this trait to spread.

Keywords: competition, epidemiology, manipulation of parasites, R_0, sociobiology, spite.

INTRODUCTION

One of the most antagonistic associations in the natural world is that between a parasite or pathogen and its host. Parasites (or pathogens, henceforth used interchangeably) and their hosts are expected to have conflicting interests, simply because parasite reproduction and transmission are performed at the expense of the host's fitness. However, this may not always be the case. In fact, infected hosts can use their parasites as biological weapons to *harm* susceptible non-kin hosts, and increase their own relative fitness. This possibility will be investigated here.

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The evolution of harmful behaviour – selfish and spiteful behaviour – is the subject of a classic paper by Hamilton (1970). According to Hamilton, 'behavior which harms others without benefit to the self may well be called "spiteful" . . . Of intraspecific cases it is doubtful if any can be considered confirmation of the present model. "Merely selfish" interpretations are too readily available'. The difficulty of identifying examples of spiteful behaviour is expressed by Hamilton as follows: 'But why, if the model is correct, are more convincing examples of spite hard to find?' (see also Hurst, 1991; Gadagkar, 1993; Keller *et al.*, 1994; Foster *et al.*, 2001). Hamilton suggests three reasons for that: (i) spiteful actions 'do cost something'; (ii) 'an animal will not normally have any way of recognizing which other members of its species have less than average relationships'; and (iii) 'single populations that are so small (. . .) as to have [a high probability of identity between the spiteful individual and a random individual in the population] must be in a precarious position already, and the selection of a gene causing spite can only hasten their extinction' (Hamilton, 1970). I argue here that parasites could play the role of spiteful weapons among hosts, hence escaping Hamilton's three objections.

Consider individuals of a given species, among which some are infected by a given parasite. Infected hosts would re-transmit the parasite to susceptible hosts with a given probability. Consider now a *harmful* mutant. When infected by a parasite, that mutant is willing to pay a certain fitness cost to increase the probability of passing the parasite to non-kin susceptible hosts. Despite such fitness cost to the mutant, the 'recipient' of the pathogen or of the parasite would suffer a considerably higher fitness cost – and one expects this to be true for many, if not most, parasites/pathogens. That is, since the host is already infected, the cost of infecting other hosts may be very low. This argument would address the first objection of Hamilton. Increasing the transmission of a parasite or pathogen towards other individuals would be expected to be too risky for the actor and for its kin members. However, for many diseases, immunity enables a kind of 'recognition' mechanism, hence preventing the pathogen from infecting or seriously harming the actor or its kin members. For example, there are viruses integrated in bacterial chromosomes that are in a *dormant* stage. These viruses are inactive in the sense that they are replicated only during the replication of the bacterial chromosome. Therefore, if a given bacterial cell harbours one such virus, its descendants also harbour a copy of this virus. Moreover, for several types of viruses, once integrated in a bacterial chromosome, the cell does not allow the entrance of a similar virus. And this is why immunity may allow a kind of recognition mechanism of non-kin members. Similarly, immune systems (adaptive or not) allow hosts of a given family to recover from a given disease, while non-related hosts would die of the same infection. Therefore, for many host–parasite and host–pathogen dyads, these immunity systems solve the second objection of Hamilton: hosts may have difficulties in recognizing their kin members, but their immunity systems often facilitate this requirement. Hamilton himself provided a solution for the third objection: he suggested the existence of a 'composite population' of spiteful individuals made up of many sub-populations with migration between them. Indeed, as Hamilton (1970) recognized at the end of his paper, 'panmixia hardly occurs'. That is, most species live in subdivided populations. With the three objections solved, one might expect that by directing the pathogen or the parasite towards non-kin hosts, this harmful trait would increase the relative fitness of their actors or kin members (also carriers of the mutant allele).

Here, I present a mathematical model for the selection of infectious hosts. I then try to provide the tools to predict the most likely biological systems in which such behaviour can

occur. Mechanisms of infection or transmission depend significantly on several factors, pertaining either to the host or parasite species or to the environmental conditions where the interaction occurs. In this paper, I focus on a specific case of host–parasite dyad, that of bacteria and their viruses.

MODEL

Hamilton's rule and the evolution of altruism

Evolutionary biologists consider that individuals (i.e. the actors) who change the fitness of their conspecifics (i.e. the recipients) are performing a social interaction. Selection of social traits depends on: (i) the consequence to the fitness of its actor; (ii) the consequence to the fitness of the recipient; and (iii) the relatedness between actors and recipients. Since the paper by Williams and Williams in 1957 and the publication of Hamilton's rule in 1963, many evolutionists have tried to describe the necessary conditions for the selection of altruism.

According to Hamilton's rule, altruism is favoured when

$$Rb - c > 0 \tag{1}$$

where b is the benefit to the recipient of the altruistic act, c is the cost to the actor, and R is the relatedness of the actor to the recipient (Hamilton, 1963, 1964). The generality of this equation, the meaning of each of its terms, and how one should calculate relatedness are topics of widespread research (see, for example, Grafen, 1985; Frank, 1998; Rousset, 2004).

In 1992, using computer simulations, Wilson and colleagues showed that, in viscous populations (characterized by limited dispersal without any global mixing stage), competition between kin individuals is exactly opposite to the favourable role of relatedness in the selection of altruism (Wilson *et al.*, 1992). In the same year, two analytical models by Taylor showed that the two effects cancel each other out, both in patch- (Taylor, 1992a) and homogeneous-structured populations (Taylor, 1992b), irrespective of the dispersal rate. Therefore, it is not the overall mixing of the population that governs the altruistic threshold, but the timing of the social interaction in a life cycle that alternates breeding with dispersal (Taylor, 1992a, 1992b). Therefore, models involving Hamilton's rule have to take into account the life cycle of individuals implicated in social interactions. Queller (1994) showed that one has to perform a proper calculation of relatedness in structured populations (Grafen, 1985; Queller, 1994; Frank, 1998; West *et al.*, 2001, 2002; Gardner and West, 2004; Gardner *et al.*, 2004; Griffin *et al.*, 2004). In a way, the models of Taylor (1992a) and Queller (1994) could play a role as null models to which one compares new results. For example, by changing the life cycle of Taylor (1992a) from 'social interactions ⇒ breeding ⇒ dispersal ⇒ competition' to 'breeding ⇒ social interactions ⇒ dispersal ⇒ competition', altruism may evolve because social interaction occurs between siblings while competition occurs with average members of the population.

Selfish and spiteful behaviour

According to the signs of b and c in Hamilton's rule, social behaviours are classified as selfish if $c < 0$ and $b < 0$ and as spiteful if $c > 0$ and $b < 0$ (Hamilton, 1964, 1970).

A necessary condition for spiteful behaviour to be selected is that its actor directs damage towards individuals less related than the average competitor of the actor – including the

actor (Hamilton, 1970, 1971, 1975; Foster *et al.*, 2001; Gardner and West, 2004). Spiteful behaviour evolves because it reduces the frequency of rival alleles. In the context of this paper, an infected host may pay a certain amount of his fitness to be more harmful to a non-kin host – precisely by increasing the probability that the latter is infected.

The theoretical definition of spiteful behaviour and the relation between Hamilton's spite and Wilson's spite (Hamilton, 1970; Wilson, 1975) has been the subject of some debate, mainly in recent years (Foster *et al.*, 2000, 2001; Gardner and West, 2004; Lehmann *et al.*, 2006; Gardner *et al.*, 2007). In particular, some authors define a harmful behaviour as spite if it has a negative effect on the actor's personal fitness, whereas others focus on the negative effect on the actor's fecundity. This distinction is important because, if the reduction in the number of offspring generated by the actor and by the recipient reduces competition among offspring, the number of the actor's descendants reaching adulthood may increase; in that case, this behaviour would be considered as selfish and not spiteful (Hamilton, 1970; Lehmann *et al.*, 2006; Vickery, 2003; see also Gardner *et al.*, 2007; West *et al.*, 2007).

In the rest of this section, I follow Taylor (1992a) and, in part, a simple model by Lehmann *et al.* (2006) and derive the inclusive fitness effects directly. Individuals live in an infinite island model (Wright, 1943). That is, the population is made up of an infinite number of demes, each with N adults after regulation. Individuals are haploid and generations do not overlap. The number of adults is fixed – due to some exterior imposition. Therefore, an increase in the number of adult progeny left by one class necessarily implies a decrease in the number of adult offspring left by another class. In other words, the effects on the fitness of *all* adults sum to zero:

$$-c + b_0 + b_1 = 0 \tag{2}$$

In this equation, $-c$ is the effect of the offspring's trait on the fitness of the focal adult, b_0 is the effect of the offspring's trait on the fitness of $N-1$ other adults from the same deme, and b_1 is the effect of the offspring's trait on the fitness of adults from other demes (Rousset, 2004; Rousset and Billiard, 2000).

Because of the assumption that one has an infinite number of demes, the probability of genetic identity between the mutant and an individual in another deme is zero. Because individuals are haploid, the probability of genetic identity between two homologous genes randomly sampled from any given individual, including the focal individual, is equal to one. Therefore, the inclusive fitness (IF) effect of the focal individual is given by:

$$\Delta W_{\mathrm{IF}} = -c \cdot 1 + b_0 \cdot Q_0 + b_1 \cdot 0 \tag{3}$$

Therefore, the condition $\Delta W_{\mathrm{IF}} > 0$ implies that

$$-c + b_0 \cdot Q_0 > 0 \tag{4}$$

In this equation, Q_0 represents the probability of genetic identity between the focal individual and any other individual of the same deme. For Wright's infinite island model, the probability Q_0 corresponds to Wright's F_{ST}:

$$Q_0 = F_{\mathrm{ST}} = \frac{(1-m)^2}{N-(N-1)\cdot(1-m)^2} \tag{5}$$

where m is the migration rate (Wright, 1943).

In the model that follows, I assume that the offspring of the focal individual use a recognition mechanism to direct damage against all immigrants; in the case an offspring is himself a migrant, he damages all the other offspring (migrants and non-migrants) when he arrives in a new deme. Such harm occurs among offspring immediately *after* dispersal. The life cycle is as follows. First, each deme has N adults. All N adults breed and generate a very large number of offspring; all adults die. Second, a fraction m of progeny migrate towards a random deme. Third, offspring bearing the allele for damage harm other offspring. Fourth, in each deme, non-migrant and immigrant individuals compete for the N breeding spots. Then, the cycle begins again with the first step.

First, let us focus on the interaction that occurs at the focal deme. Suppose that after breeding there are a total of T offspring, T/N of which are descendants from the focal individual. After migration one still has a total of T offspring in each deme. Among them, $E = m \cdot T$ belong to external parents, $F = (1-m) \cdot T/N$ belong to the focal individual, and $G = (1-m) \cdot T \cdot (N-1)/N$ belong to the other parents of the focal group. After the spite behaviour, E is reduced to $E-e$, F is reduced to $F-f$, and T is reduced to $T-e-f$.

Then, at the focal deme, the overall change in fitness of the harmed parents (measured as a share of a single patch) is

$$\Delta_E = \frac{E-e}{T-e-f} - \frac{E}{T} \approx \frac{E}{T} \cdot \frac{e+f}{T} - \frac{e}{T}$$

to first order of the Taylor series around $e/T \sim 0$ and $f/T \sim 0$, assuming that e/T and f/T are small. Similarly, the change in fitness of the focal parent is

$$\Delta_F = \frac{F-f}{T-e-f} - \frac{F}{T} \approx \frac{F}{T} \cdot \frac{e+f}{T} - \frac{f}{T}$$

And the change in fitness of parents from the focal deme (other than the focal parent) is

$$\Delta_G = \frac{G}{T-e-f} - \frac{G}{T} \approx \frac{G}{T} \cdot \frac{e+f}{T}$$

Now, let us define $C \equiv f/T$ and $D \equiv e/T$.

We can now analyse what happens to the migrant spiteful offspring arriving in other demes. The total number of migrants of the focal individual is mT/N. Given that the number of demes is very high, one must assume that these migrants fall into different demes. Each of these offspring harms all the offspring (residents and migrants) present in the new deme. In this new deme, the number of harmful individuals is reduced from 1 to $1-h$, the number of the other juveniles is reduced from $T-1$ to $T-1-j$, and the total number of juveniles in this deme is reduced from T to $T-j-h$. Then:

$$\Delta_{\text{harming migrant}} = \frac{1-h}{T-h-j} - \frac{1}{T}$$

and

$$\Delta_{\text{other juveniles in new deme}} = \frac{(T-1)-j}{T-h-j} - \frac{(T-1)}{T}$$

At this point, one has to make another assumption – that the cost of being a harmful individual is the same in the focal deme as in a remote deme. That is, I assume that $h = f/F$

because there is only one offspring of the focal parent in each new deme. Therefore,

$$\frac{h}{T} = \frac{C \cdot N}{(1-m) \cdot T}$$

These interactions occur in $m \cdot T/N$ demes, which means that:

$$\frac{m \cdot T}{N} \Delta_{\text{harming migrant}} \approx -C \frac{m}{(1-m)}$$

Then, the fitness cost to the focal adult is $c \equiv \Delta_F + \frac{m \cdot T}{N} \Delta_{\text{harming migrant}}$:

$$c \approx C - \frac{1}{N} \cdot (1-m) \cdot (C+D) - C \frac{m}{(1-m)} \tag{6}$$

Finally, the effect on the fitness of other parents from the focal deme is $b_0 \equiv \Delta_G$:

$$b_0 = \frac{N-1}{N} \cdot (1-m) \cdot (C+D) \tag{7}$$

Plugging in these mathematical quantities into equation (4) gives the condition for the spread of the harming trait:

$$N < \frac{D}{C} \cdot \frac{(1-m)^2}{(2-m) \cdot m} \tag{8}$$

If the benefit of reduced competition is high enough, then $-c > 0$, and this harming trait is a selfish behaviour (competition). If $-c < 0$, then this harming trait is a spiteful behaviour. Therefore, the full condition for the spread of spiteful mutants is

$$(1-m)^2 \cdot \left(1 + \frac{D}{C}\right) < N < \frac{D}{C} \cdot \frac{(1-m)^2}{(2-m) \cdot m} \tag{9}$$

According to equation (8), rare harming mutants cannot invade a population of non-harming individuals. For example, if $C = 0.1$, $D = 0.2$, and $m = 0.1$, equation (8) states that N has to be less than ten individuals, a very unrealistic condition for social living beings.

It is likely that common harmful behaviours – such as physical attacks – cause fitness costs to their actors that are of the same order as the costs to their recipients. In the example just given, $D/C = 2$. In the next section, I argue that if selfish or spiteful behaviour involves viruses, bacteria or other biological weapons, then the ratio D/C may be several orders of magnitude higher than in the previous example. Therefore, one should be able to find many examples of spiteful behaviour by looking at host–parasite relationships.

Spiteful and selfish hosts: an example

A *general* model in which hosts use their pathogens to harm other individuals is more complex than the situation just presented, not to mention that it depends on the parasite/pathogen and the host involved. A model may also consider the existence of infected hosts, recovered hosts or immune hosts. Depending on the cost of being infected, individuals may

die or recover and become susceptible again. Therefore, in this section I focus on a specific dyad, that of a virus infecting bacterial cells.

Bacteria have several types of viruses (also called bacteriophages or simply phages). There are DNA and RNA phages. Some phages have single-stranded or double-stranded genomes, spanning between 4 and 200 genes. Some phages kill every cell they infect; others are temperate, which means that they are able to integrate themselves into the bacterial genome as dormant 'prophages', also called lysogens (for a review, see Campbell, 1996). Let us focus on the temperate lambda phage, a virus that infects *Escherichia coli* bacterial cells. This phage is probably the 'most thoroughly investigated temperate phage' (Campbell, 1996) and was fundamental to the main developers of molecular biology, such as A. Lwoff, M. Delbruck, J. Monod, F. Jacob, and M. Radman, among others. Another reason to choose this phage is that it has similar properties to many other phages that also infect *E. coli* or other bacterial species (e.g. P22 that infects *Salmonella*).

Upon infection of an *E. coli* cell by a lambda phage, one of two things can happen. The first is phage production for about 35 min and then cell lysis with a burst size of 100 new phages ready to infect new *E. coli* cells. Alternatively, an infected host may survive by harbouring the phage genome in a latent form (prophage). Only rarely is the phage DNA excised from the chromosome; when this stochastic event takes place in a given bacterial cell, there is massive phage production and about 100 new phages come out from the cell, killing it. Moreover, cells containing these prophages can no longer be infected by the same phage.

In what follows, the λcII$^-$ mutant is considered. This mutant phage cannot establish itself as a prophage (dormant stage); this means that, upon entry into *E. coli* cells, these phages always proceed to phage production and host killing (Campbell, 1996).

A bacterial cell containing one of these latent phages has at least the same growth rate as its isogenic phage-free counterparts (Edlin *et al.*, 1975). In this model, I follow the conservative assumption that latent phages do not change their bacterial growth rate. Therefore, a deme with one of these cells has the same fecundity as a deme completely free of these phages or prophages.

Let us consider a bacterial cell that receives a lambda virus and that this virus integrates into the bacterial chromosome. Then this cell replicates several times, and all descendant cells harbour the dormant virus in the chromosome. If, for any reason, in one of these cells the virus stops being dormant and starts replication, the cell eventually dies and about 100 lambda viruses arise. The entry of these viruses into another cell already harbouring a similar virus is inhibited; in contrast, they can also enter a bacterial cell free of this virus. In this way, a bacterial cell that produces lambda viruses can distinguish kin from non-kin members because these viruses do not infect bacterial cells already harbouring the dormant virus. Suppose that each deme contains, for example, 10^4 cells, one of them being a mutant containing the λcII$^-$ phage. Then, all cells duplicate 20 times, reaching $10^4 \times 2^{20} \cong 10^{10}$ cells. Each cell, including the mutant, has now about a million descendants, after which a proportion m disperses towards other demes. Then, suppose that one in a million *E. coli* carriers of the phage starts phage production and then kills its host (as assumed in the model, $h = f/F$, which means that the cost to the harming individual does not depend on the number of individuals available to harm). The burst size, β, of this phage/bacteria dyad is around 100 viral particles. That is, an infected cell infected by lambda phages produces $\beta = 100$ phages, each one ready to infect another 100 *E. coli* cells. After these two rounds, about $\beta^2 = 10^4$ bacterial cells die. The cost to the harming host is its own death. The cost, d,

to one recipient of each of these viruses is also its death. Therefore, C and d are similar, but a total of $\beta^2 = 10^4$ bacterial cells die. Therefore, in this case: $D/C = d \cdot \beta^2/C \approx \beta^2 = 10^4$. Then, with $m = 0.1$, equation (9) tells us that there is selection for this harmful behaviour mediated by the λcII$^-$ phage if the number of bacterial cells in the deme is lower than 42,631; moreover, one would classify this as spiteful behaviour if $-c < 0$, that is if $N > 8100$. Therefore, for a population size of $N = 10^4$, this virus-mediated bacterial behaviour can be considered spiteful.

Epidemiology and the evolution of spiteful and selfish hosts

In the example given above, the cost to the host is its own death. The cost to one recipient of each of these viruses is also its death. However, in many cases, the cost of infecting other hosts is much lower than the cost of being infected. The trait considered here is that of directing the parasite to non-kin. Therefore, if one assumes that the baseline fitness of mutants and wild-type hosts already encompasses a given probability of being infected by the parasite, the fitness cost C would correspond solely to the cost of directing the parasite to non-mutants and D to the increasing probability of being infected times the cost of being infected by such a parasite. Therefore, we can assume that, in general, C is much lower than D.

Putting the argument in an epidemiological context, one may speculate that the number of viral particles or any other parasite coming out from a host increases with the basic reproductive ratio R_0. This number, R_0, is defined as the expected number of secondary infections arising from a single individual during his or her entire infectious period, in a population of susceptible hosts (Anderson and May, 1999; Heffernan *et al.*, 2005). Moreover, each of the recipients of the parasite may once more infect other recipients; and this may occur t times. Therefore, one may expect D to be proportional to $C \cdot (R_0)^t$, where t is greater than one. Therefore, equation (9) becomes:

$$(1-m)^2 \cdot (1 + (R_0)^t) < N < (R_0)^t \cdot \frac{(1-m)^2}{(2-m) \cdot m}$$

DISCUSSION

This paper had two main goals: (1) to argue that living beings may use their parasites as selfish or spiteful weapons, and (2) to argue that spiteful behaviour should be much more common than initially predicted by Hamilton (1970). I did this by addressing directly Hamilton's three objections for the evolution of spiteful behaviour: (i) small costs to the actor (compared with the cost to recipients); (ii) recognition between spiteful 'animals'; and (iii) living beings for which spiteful behaviour is about to evolve should be living in subdivided populations. The responses to these three objections are as follows:

First, contrary to Hamilton's expectations, the ratio cost to actor/cost to recipient(s) may, nevertheless, be very low. This can be accomplished if several parasites or pathogens arise from a single host; moreover, the cost of directing the infection from kin to non-kin susceptible hosts does not increase significantly when potential recipients increase. Finally, an infected 'non-spite' host can then propagate this effect by re-transmitting this parasite towards other wild-type hosts.

Second, animals may have difficulty recognizing kin and non-kin members. However, many 'immune systems' may play the role of recognition without *cognition*. For example, it is often the case that a virus that is already inside a cell does not allow a similar virus to enter (as is the case of lambda viruses infecting bacteria). In general, molecular 'recognition' among microbes is one of the main reasons why microorganisms are interesting subjects for the study of social evolution (Axelrod and Hamilton, 1981; West *et al.*, 2006). Moreover, immunity among vertebrates may prevent infection among kin members. Indeed, smallpox, measles, influenza, and other infectious 'diseases endemic in Europe played a decisive role in European conquests, by decimating many peoples on other continents' (Diamond, 1999, pp. 77–78).

Third, as Hamilton had already mentioned, probably all species live in subdivided populations, not in a single panmictic population.

For these conditions to be sufficient for a spiteful allele to be selected, the value of D/C should be much higher than one (condition (i)). High values of D/C could be attained if the number of parasites/pathogens arising from a host is high. Is this always accomplished? If at some evolutionary time point this value is low, natural selection acting on the parasite alone will cause an increase in the basic reproductive ratio, R_0. Such evolution may occur long before equations (8) and (9) are satisfied, after which the evolution of spiteful behaviour among hosts may take place. Indeed, although the condition for the maintenance of a parasite is that $R_0 > 1$, it is clear that R_0 of many pathogens has reached values well beyond 1. For example, the R_0 of measles in England and Wales between 1950 and 1968 was between 16 and 18 (Anderson and May, 1999, and references therein). R_0 is best quantified in simple systems, such as viruses infecting bacteria. The number of viruses released by a bacterial host is usually high. For example, an *E. coli* cell infected by the M13 virus continuously releases 100–200 replicated viruses per generation and about 10,000 or more phages exit from an *E. coli* infected with the phage MS2 (for a review, see Campbell, 1996); each of these new viruses is able to infect a new bacterial cell.

Some authors have argued that infected hosts may use their parasites to fight non-kin individuals. Unfortunately, this argument has received little attention from parasitologists and epidemiologists. For example, in 1992, Watve (cited in Jog and Watve, 2005) suggested that elephants, being nomad animals, might contaminate water holes with feces after using the water – probably a costless behaviour. This behaviour would have been selected because other elephants, by passing later through the same area, could become infected with their parasites. Being nomad animals, defecation in these waters does not infect members of their kin group. Rozsa (2000) also analyses the hypothesis, giving several examples of hosts/parasites where this phenomenon could occur. Mallon and Schmid-Hempel (2004) showed that there is a negative relationship between the rate of contact between worker bumblebees of two colonies in a behavioural assay and their respective distance in susceptibility to different strains of pathogens. Possibly, worker bumblebees may be trying to pass disease on to non-kin bumblebees (Mallon and Schmid-Hempel, 2004). Finally, in an interesting paper on the ecology of microbial invasions, Brown *et al.* (2006) argued that, compared with toxins (bacteriocins), viruses (bacteriophages) would be useful as biological weapons for some bacteria to displace other bacteria in habitats such as mammalian guts – precisely because of the capacity of viruses to replicate themselves inside their victims (Brown *et al.*, 2006). These papers and others (see, for example, Dionisio, 2005) highlight the importance of parasites for competition and maintenance of diversity. But these papers do not situate the problem in an evolutionary perspective, only in an ecological approach.

A mathematical treatment of this evolutionary hypothesis and its analysis as a case of evolution of spiteful behaviour (Hamilton, 1970) was absent until now. A theoretical analysis – such as that presented here – in its proper framework may help to determine the conditions for this hypothesis to be regarded as a fundamental feature in epidemiology and evolutionary epidemiology.

Experiments designed specifically to test the hypothesis that infected hosts may collaborate with their parasites/pathogens to help their transmission – in an evolutionary and not just ecological framework – have yet to be conducted. However, as the interests of hosts and parasites are (at least partially) aligned, how should one distinguish host collaboration from parasite selfishness?

The equations in this paper and our knowledge of behavioural ecology give us the necessary framework to distinguish the two forces. For example, one could distinguish host spiteful behaviour from parasite selfishness by looking to host–parasite systems in which the cost D is different to the two host sexes. For example, to men, the cost of getting mumps may be much higher (testicular atrophy in some cases) than to women. Hence, if the spread is mediated by the host's harming behaviour, one would expect mumps to be more frequent in men than in women, whereas if the spread is controlled by the parasite, mumps should be equally frequent in men and women.

More examples can be derived from our knowledge of sociobiology and behavioural ecology. First, consider a given host species whose members of one sex compete more intensively for mates [usually males (but see, for example, Clutton-Brock and Vincent, 1991; Clutton-Brock *et al.*, 2006)] than members of the other sex (Trivers, 1972; Andersson, 1994). According to the hypothesis presented here, one should expect pathogen-mediated spiteful acts to occur more often among the former than among the latter members. However, such differences in infectious spiteful behaviour should come to an end after the reproductive age of individuals. Another case in which there should be no difference between the sexes is that in which the pathogen is spread by a vector (e.g. malaria in humans). As a final example, consider a given act suspected of having the objective of spreading pathogens among conspecifics. Then, this act should be observed among members belonging to social rather than non-social species. This should be tested with two very close host species, one social and the other asocial.

The hypothesis that infected hosts may collaborate in parasite transmission to increase hosts' relative fitness should be tested experimentally. If confirmed, this could have serious consequences for the epidemiology of several diseases, as it may profoundly affect estimates of disease transmission.

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