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Adaptation and enslavement in endosymbiont-host associations

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The evolutionary persistence of symbiotic associations is a puzzle. Adaptation should eliminate cooperative traits if it is possible to enjoy the advantages of cooperation without reciprocating—a facet of cooperation known in game theory as the Prisoner's Dilemma. Despite this barrier, symbioses are widespread and may have been necessary for the evolution of complex life. The discovery of strategies such as tit-for-tat has been presented as a general solution to the problem of cooperation. However, this only holds for within-species cooperation, where a single strategy will come to dominate the population. In a symbiotic association each species may have a different strategy, and the theoretical analysis of the single-species problem is no guide to the outcome. We present basic analysis of two-species cooperation and show that a species with a fast adaptation rate is enslaved by a slowly evolving one. Paradoxically, the rapidly evolving species becomes highly cooperative, whereas the slowly evolving one gives little in return. This helps understand the occurrence of endosymbioses where the host benefits, but the symbionts appear to gain little from the association.

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I. INTRODUCTION

Cooperation between endosymbionts and their hosts is most striking in the common case where the symbiont can survive in a free-living form and each host is infected anew in its infancy [1–3]. If the host is unable to respond to individual symbionts who do not contribute to the association, then free riders will prosper and the symbiont will ultimately become parasitic on its host [4,5]. On the other hand, if the host is able to punish defecting symbionts, the expectation is that a "you scratch my back, and I'll scratch yours" relationship will develop [6,7]. It is supposed that the reciprocation of both cooperation and defection maintains a mutualistic relationship, from which both parties benefit. This appears to be supported by game-theoretic analyses of simple models of cooperation, with tit-for-tat strategies being successful in Prisoner's Dilemma scenarios [8–10]. Although tit-for-tat emerges as the winning strategy under a wide range of conditions, most studies of cooperation are restricted to intraspecific competition. It is not clear that this can be generalized to the host-endosymbiont system, where the Prisoner's Dilemma occurs between two species.

In natural systems, it is found that many horizontally transmitted nonobligate endosymbionts apparently generate large benefits for their hosts. Examples include nitrogen fixation by rhizobial bacteria in legumes [11]; enhanced uptake of nutrients due to mycorrhizal fungi [12]; carbon uptake by green algae in many aquatic invertebrates, such as the zooxanthellae of corals [13]; and bioluminescence provided by bacteria in squid and fish [14]. Surprisingly, in very few cases have endosymbionts been shown to benefit significantly from their interactions with host organisms [15]. For example, *Rhizobia* reproduce happily enough when free living in the soil, but most of these bacteria hardly reproduce at all once inside the root nodules of legumes [11,16]. For the putative benefits of symbiotic life as zooxanthellae, dinoflagellates give up their cell wall and their flagella, sacrifice most of their photosynthetic products, and reduce their reproductive rate [17]. The nonobligate forms of endomycorrhizal fungi can be readily grown alone, and there is no evidence for a fitness-related benefit from symbiosis for them [12]. In particular, there is no evidence that carbon flows from the plant to the fungus in return for the nutrients these endosymbionts provide. Thus notions of host and parasite appear to be turned on their head, and this asymmetry is not explained by the standard tit-for-tat solution to the problem of cooperation.

Most previous models of cooperation have only represented one population. In this paper we present a simple model of a two-species association based on reciprocal altruism, and explore whether it can explain both the maintenance of symbiotic relationships and the apparent enslavement of the symbionts by their hosts. In keeping with much previous work on the evolution of cooperation, we formalize the Prisoner's Dilemma in terms of the costs, c and benefits b of cooperative acts. The species have variable degrees of cooperation, depending on the value of these parameters [18–21]. The degree of cooperation adopted by each species is subject to evolutionary change. The challenge is then to demonstrate that a mutualistic relationship is stable in the face of mutations in the parameters governing cooperation.

A core asymmetry between the host and the endosymbionts is that the symbionts have a shorter generation time. This rapid turnover allows their population to respond quickly to changes in the hosts' behavior. A consequence of this differential adaptive rate is that the tit-for-tat strategy is no longer optimal. Rather the endosymbiont becomes fully

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cooperative and the host becomes miserly, adopting a level of cooperation just high enough to maintain the symbiont cooperation. The differential rates of adaptation appear to lead directly to the differential payoffs inferred from studies of host-endosymbiont systems.

II. MISERS AND SLAVES

In this section we consider just a pair of agents that interact to illustrate the idea that a slower rate of adaptation can be advantageous. This appears closely related to the Red King effect [22], although that model specifically avoids treating the Prisoner's Dilemma scenario, in which there is a constant temptation to defect on cooperative agreements. In later sections we apply this notion to a model of endosymbiosis.

Consider two agents S and H; later we will interpret these as symbiont and host. Suppose that S adopts some behavior to a degree s at a cost to itself of c_s per unit and a benefit to H of $b_{s\to h}$ per unit. For example, this could be nitrogen fixation by Rhizobia which makes nitrogen available to legumes in a useful form, but which entails a metabolic cost to the Rhizobia. Suppose that H can also adopt some behavior h between 0 and 1. This benefits S by $b_{h\to s}$ at a cost of c_h per unit. The net payoff to S from the association is then

$$w_s = b_{h\to s}h - c_s s, \tag{1}$$

while that to H is

$$w_h = b_{s\to h}s - c_h h. \tag{2}$$

For the purposes of our model we take s and h to be bounded below by 0 and above by 1. That is, we assume there is some natural limit to the amount of help that one organism can provide another. If benefits exceed costs for both parties, the maximum total payoff, w_s+w_h, is achieved when both s and h are at their maximum values. However any nonzero s or h only benefits the other party, and so is an altruistic act of cooperation. By reducing the level of cooperation, an agent reduces the costs, and so there is an incentive for each agent to defect. This selfish behavior results in the payoff to each agent decreasing and we have what is known in game theory terms as a Prisoner's Dilemma [7].

To provide an incentive for S to cooperate, H's behavior needs to depend on s in some way, and the simplest nontrivial contingency is linear, $h=H_0+(H_1-H_0)s$. Here H_0 is the response to complete defection $(s=0)$ and H_1 is the response to complete cooperation $(s=1)$. Parameters H_0 and H_1 lie between 0 and 1, ensuring that h also lies in this range. The difference H_1-H_0 can be thought of as the "responsiveness" of H. Completely unresponsive agents have $H_0=H_1$, extreme cases being the naive cooperator Always Cooperate (1,1) and the stalwart defector Always Defect (0,0). For unresponsive agents, h is independent of s and the gradient $\partial w_s/\partial s$ is $-c_s$, so S is motivated to decrease its level of cooperation. In contrast, the tit-for-tat strategy $(H_0,H_1)=(0,1)$ is as responsive as possible (see Fig. 1). In this case we have $h=s$ and $\partial w_s/\partial s=b_{h\to s}-c_s>0$, so S should cooperate more to increase its payoff. Notice that this argument does not depend on specifying the details of S's strategy (meaning the way it arrives at the value s, given h)—it merely indicates whether S should increase or decrease the level of cooperation it adopts in pursuit of greater payoffs.

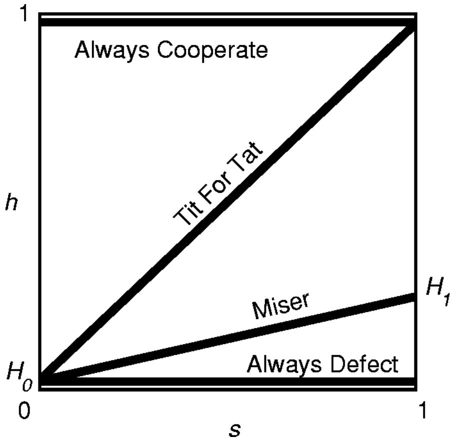

FIG. 1. Linear reactive strategies for H. Each line is a possible mapping from s to h, parametrized by H_0 and H_1.

More generally, substituting the expression for h into the payoff for S and differentiating with respect to s shows that S is motivated to cooperate as much as it can, provided that the following "incentive condition" is met:

$$H_1 - H_0 > \frac{c_s}{b_{h\to s}}. \tag{3}$$

This defines two regions on a plot of H_1 versus H_0 (see Fig. 2). If H's responsiveness is too low, S would benefit from lowering its level of cooperation, while if H's responsiveness is above the threshold $c_s/b_{h\to s}$, S should become as cooperative as it can. Now consider a scenario in which S adapts its strategy over time in pursuit of higher payoffs. If the incentive condition [Eq. (3)] is not met, s will decrease to zero. In particular, any flat response $(H_0=H_1)$ by H will lead to pure defection by S, and consequently cannot account for the persistence of a mutualistic association between them. Conversely, if the incentive condition is met, s will rise to 1.

Now consider the effect of this on H. The payoff to an H agent whose responsiveness is above the threshold will be $b_{s\to h}-c_hH_1$ (since $s=1$), compared to $-c_hH_0$ for an H below the threshold (since then $s=0$). Since benefits outweigh costs $b_{s\to h}-c_hH_1>0$ and so all H strategies above the threshold out-compete those below it. The best possible strategy for H will be the one with lowest H_1 that still obeys the incentive condition. This strategy has $H_0=0$ and H_1 just above $c_s/b_{h\to s}$ (it needs to be just above to ensure a strictly positive gradient for s). Equivalently, the optimal strategy for H is to cooperate with S at a level

$$h_{\text{miser}} = \left(\frac{c_s}{b_{h\to s}}s\right)^{+}, \tag{4}$$

where the superscript (+) means "just above." The conclusion is that the best strategy to adopt when faced with an optimally adaptive coplayer is that of a "miser." The miser

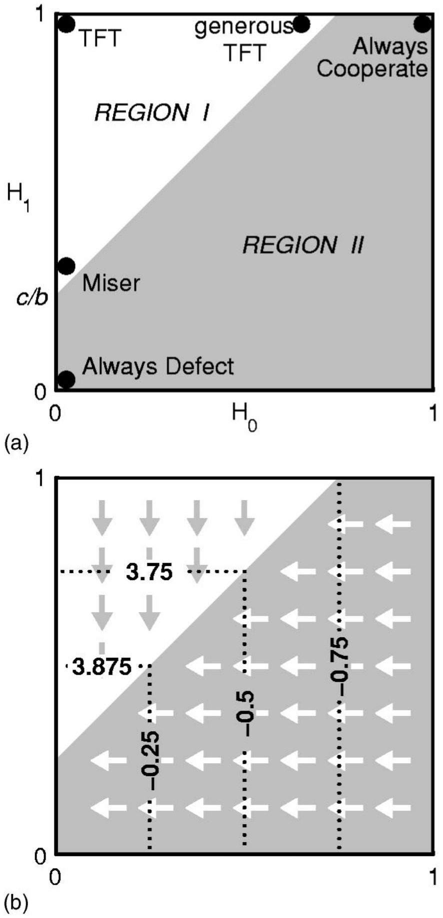

FIG. 2. (a) The space of strategies for H. Inside region I (unshaded) we have $H_1 - H_0 > c_s / b_{h\to s}$, which means that the optimal reply strategy is complete cooperation. In region II (shaded) the opposite holds, leading to pure defection. The dots mark the positions of named Prisoner's Dilemma strategies. (b) The payoff for H, plotted on the same axes, assuming that S is adaptive enough to adopt the optimal reply behavior. Contours (dotted lines) show H's payoff and arrows show the direction of steepest ascent. The numbers shown are for the specific case of $c=1$, $b=4$ for both parties. The point on this surface with the highest payoff corresponds to the miser strategy of $[0,(c_s/b_{h\to s})^+]$.

reacts with just enough cooperation to encourage the other agent to cooperate more. With H_1 at $c_s/b_{h\to s}$ the miser collects a payoff of $b_{s\to h} - c_s c_h / b_{h\to s}$, which is not much less than the maximum payoff of $b_{s\to h}$ obtainable by pure defection against the sucker strategy Always Cooperate. By contrast, the highly adaptive agent is induced to cooperate at the maximal level and for this receives a payoff only marginally above 0. If H is able to adapt but does so at a significantly lower rate than S, we might expect a miser-slave relationship to arise and be stable. This phenomenon has been noted in simulations of the Prisoner's Dilemma, although in that case the model involved was not amenable to analysis [23].

It might be argued at this point that the preceding model is biased, in that the H strategies are responsive whereas S just assumes a fixed level of cooperation. The S's are not given access to the same repertoire of strategies as the H strategies, and so perhaps their enslavement is due merely to this built-in deficiency. To show that it occurs in the same way when *both* players may change their strategies, we introduce the parameters S_0 and S_1. The level of cooperation is $s = S_0 + (S_1 - S_0)h$ and we have a simple linear dynamical system in which h depends on s, which depends on h itself. The dynamics have a single attractor that is approached rapidly, regardless of whether h and s are updated synchronously or asynchronously [18]. This point is

$$h^* = \alpha[H_0 + S_0(H_1 - H_0)], \tag{5}$$

$$s^* = \alpha[S_0 + H_0(S_1 - S_0)], \tag{6}$$

where $\alpha = [1 - (H_1 - H_0)(S_1 - S_0)]^{-1}$. Geometrically, the point (h^*, s^*), is simply the intersection of the two strategies plotted on the unit square. In Fig. 1, an S strategy maps h back to s and must be a line from the top of the figure to its base, crossing the H strategy at one point. Successive updates move the joint state towards this intersection point and convergence to equilibrium is rapid (e.g., of the order of 10–20 responses). The final levels determine the payoff that agents receive, namely,

$$w_h^* = b_{h\to s} s^* - c_h h^*, \tag{7}$$

$$w_s^* = b_{s\to h} h^* - c_s s^*, \tag{8}$$

and similarly for S. If the player S evolves its strategy sufficiently rapidly, then it is straightforward to show that the incentive condition is unchanged by this extension.

III. HOSTS AND SYMBIONTS

So far we have discussed just two agents and assumed that both adapt their behavior, with one of them (S) adapting much more rapidly. It is interesting to speculate whether this phenomenon might occur between two coevolving populations, and specifically between hosts and their endosymbionts. In an endosymbiotic relationship, the life span of the host is longer than that of the symbiont. Each of the partners generates payoffs via interactions with the other type, yet uses these to competitively replace only their own type. A single host typically contains many endosymbionts, and these replicate within the host for many generations. In the remainder of this paper we use computer simulations to explore the idea that the preceding analysis of agents H and S applies similarly to hosts and endosymbionts. The intent is not to present a detailed model of a specific host-endosymbiont system, but to examine in general terms whether this mechanism can be applicable.

Our model (shown schematically in Fig. 3) is intended to capture the simplest aspects of endosymbiotic associations. We assume purely horizontal transmission of symbionts, since this is the situation that is most puzzling. Each host organism acquires endosymbionts from the environment at some point in its early life, and a symbiotic association is formed anew with each generation. The host harbors its symbionts for some period, during which the symbionts reproduce with mutations. We assume that symbionts compete for limited resources within each host, leading to traits associ-

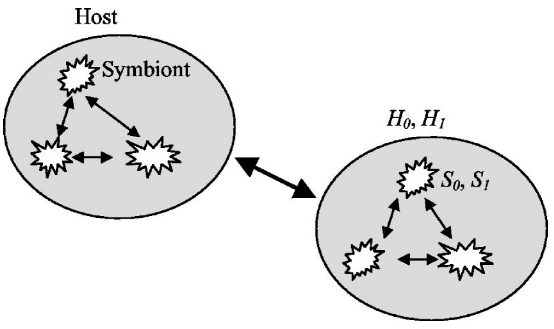

FIG. 3. Hosts and their endosymbionts. Hosts compete with hosts, and symbionts compete with other symbionts in the same host, as indicated by the arrows.

ated with greater symbiont payoffs becoming more prevalent over time. Hosts are also in a competitive environment, albeit one that occurs over a longer time scale. For simplicity we assume that variations in fitness are due solely to the host-endosymbiont association.

Specifically, we model a population of 100 individuals of a host species denoted H, each with parameters (H_0,H_1). Each host has an exclusive association with its own population of 25 symbionts, denoted S, and each such symbiont has a strategy (S_0,S_1). In our simulations the population sizes are fixed: introducing fluctuating populations would require additional assumptions (about carrying capacities for instance).

All the evolvable parameters (H_0, H_1 for hosts and S_0, S_1 for symbionts) were started with random values between 0 and 1. Each host applied its strategy of contingent cooperation in interacting with each of its symbionts on an individual basis, resulting in payoffs as described above. For simplicity, the simulations shown here used the same costs and benefits for both types of creature ($c_s=c_h$ and $b_{h\rightarrow s}=b_{s\rightarrow h}$). A very simple model of competitive replacement was used to simulate the effect of natural selection, as follows. For symbionts, two individuals were chosen at random from a single host. The payoff to each individual was calculated using Eqs. (8), but with a small amount of random noise (uniformly distributed in the range ±0.01) being added. The symbiont with lower fitness (payoff) was then deleted and replaced by the other. Rather than perfect replication of the better strategy, mutations were introduced by adding random noise uniform in the range ±0.01 to each parameter as it was copied, while constraining them to remain within 0 and 1. This allowed new strategies to arise that were not present in the original population. Exactly the same procedure was applied to competition between hosts. We refer to N replacements, where N is the size of the relevant population, as one generation. Endosymbionts underwent 25 such generations per host replacement, and the simulation was run for 100 host generations. The fitness of a given host was taken to be the sum of the payoffs from its interactions with all its endosymbionts at the end of 25 endosymbiont generations. Each new host began life with randomly generated new endosymbionts. This reflects the fact that the most difficult case to understand is horizontal transmission, where symbionts exist in a free-living form and infect hosts anew with each generation. Horizontal transmission also appears to be the most common mode of maintaining symbiont-host associations [1].

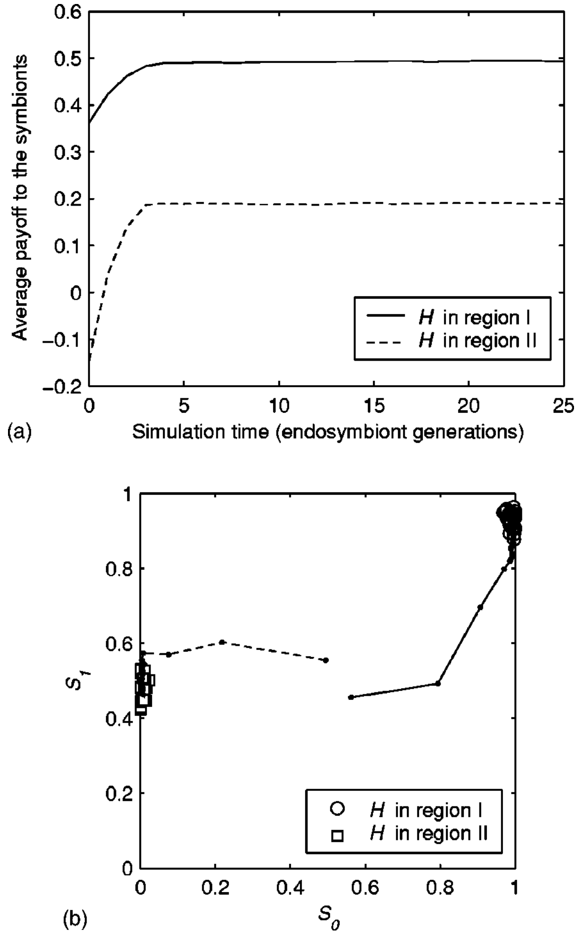

FIG. 4. Examples of the evolution of endosymbionts within a single host. The solid lines and circles show results for symbionts within a host with a strategy in region I of Fig. 2, $H_0=0.02$, $H_1=0.15$. The dashed lines and squares show results for a symbionts associated with a host in region II, $H_0=0.02$, $H_1=0.05$. (a) A timeline of the average payoffs received by the symbionts. (b) The evolution of the symbiont strategies, showing the trajectory of the mean values of the parameters S_0 and S_1. The symbols show the strategies at the end of the 25 generation simulation. There is initially a rapid change in S_0, followed by a slower change in S_1.

Within each host, the symbionts evolve towards either full cooperation or defection, depending on whether the host strategy is in region I or II of Fig. 2. The examples in Fig. 4 show the evolution of the symbionts within two hosts: one slightly more cooperative than the miser strategy and the other slightly less cooperative. There is initially a rapid change in the symbiont strategies towards $S_0=1$ and $S_0=0$, respectively. The change in S_1 is slower, because in the example given H_0 is small. As expected, the payoff to the symbionts within a host increases with time.

At the end of the full simulation the miser strategy dominated the host population and most endosymbionts adopted strategies very close to unconditional cooperation (see Fig. 5). After an initial transient, lasting for around 20 host generations, the average payoff to the endosymbionts remained at less than one-tenth of the averaged payoff to the hosts.

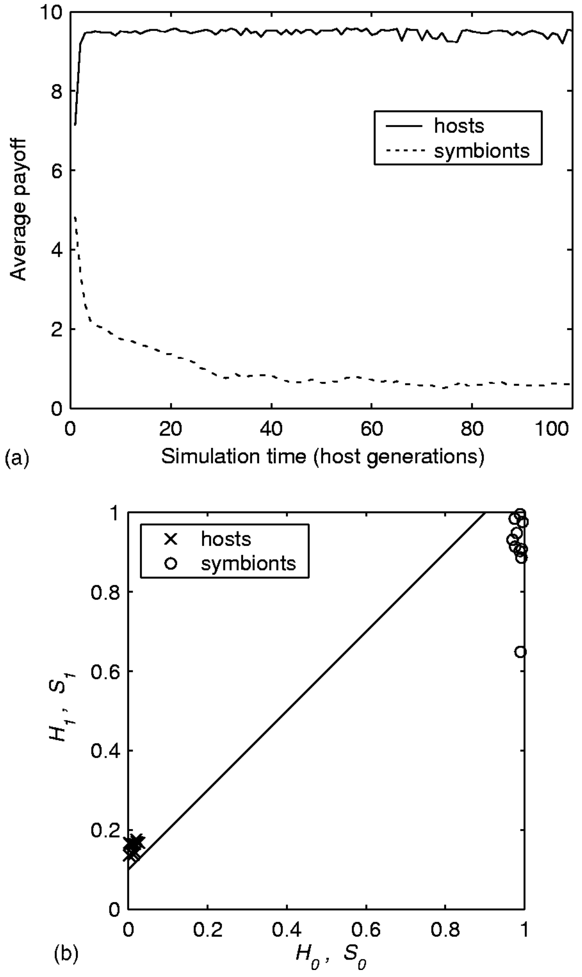

FIG. 5. Coevolution of hosts and endosymbionts. (a) A timeline of the average payoffs received by hosts and symbionts (b) A random sample of the strategies present at the end of the simulation (to be compared with Fig. 2).

Note that the payoff to the symbionts decreases as the hosts evolve. Occasionally a mutation would take a host across the boundary into the region which is too noncooperative, this host's symbionts would then stop cooperating, the payoff to the host would fall, and it would be eliminated from the population through the selection process. The asymmetry in the rewards of the association remains even at low cost-to-benefit ratios (Fig. 6). As c approaches zero there is little cost to cooperation and hence little incentive to defect, and yet the degree of miserliness becomes increasingly severe. Similar results are achieved if the symbionts do not respond to the host (i.e., if the constraint $S_0 = S_1$ is applied). In order to maintain the cooperation of the symbionts the host strategy must be responsive. In a simulation which imposed both $S_0 = S_1$ and $H_0 = H_1$ the hosts and the symbionts both rapidly adopted strategies close to All Defect, with little payoff to either party. Similarly, if the host responds not to the individual symbionts but rather to an averaged level of cooperation, then mutual defection rapidly ensues.

IV. THREE MODERATING INFLUENCES

The argument given here makes a number of simplifying assumptions, some of which accentuate the degree of miserliness. In real systems we might expect somewhat less extreme outcomes for the following reasons.

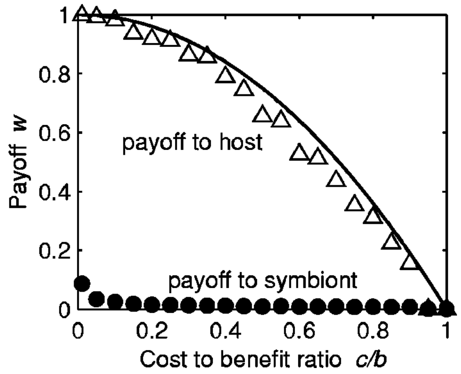

FIG. 6. The average payoffs to hosts (triangles) and symbionts (filled circles) vs the cost-benefit ratio, with $b = 1$, where both species experience the same cost and benefits. The solid line indicates the predicted payoff for miserly hosts containing fully cooperative symbionts, $b - c^2/b$.

First, the model assumes that once symbionts enter a host they are trapped there, at least until the host dies. Clearly things will be different if they are free to go. One can draw the analogy with sets of companies and their employees: for the worker there is a trade-off between staying (with poor but secure working conditions) and going in search of greater prosperity with another employer, entailing some risk associated with the transfer (i.e., the costs and risks of transit itself, and the possibility that the new host/employer is even worse). On the other hand, this implies some selection pressure in favor of barriers or other "exit costs" that hosts might be expected to impose on their workforces. For example, the "walling in" of Rhizobia in the root nodules of legumes may merely enhance the uptake of fixed nitrogen by the plant, but it also could be argued that it plays a role in preventing the bacteria from leaving.

Second, all hosts in the simulation contain the same number of symbionts. One might instead expect the carrying capacity within more miserly hosts to be lower, indirectly decreasing their fitness. In general, hosts should evolve to be as miserly as possible while still retaining sufficient numbers of sufficiently compliant endosymbionts.

Finally, the model of selection employed here is a brutal one, and this makes the division between regions I and II (Fig. 2) particularly stark. As a host approaches the miser strategy the gradient in fitness being followed by its endosymbiont population becomes flatter and flatter, and at the miser strategy itself the gradient is zero and so they spread out everywhere. If the endosymbionts are not responding strongly to the host strategy, the host's gradient disappears as well. Again we have a trade-off: a given host wants to be as miserly as possible while ensuring that differential incentives continue to encourage cooperation strongly enough.

Against these points, however, the inheritance regime used in our simulations makes it difficult for hosts to evolve cooperation in their symbionts. Here each host begins life with an assortment of endosymbionts with randomly chosen strategies. Increased levels of symbiont cooperation are never passed on—they must be evolved anew with each generation. More realistic models might allow the new generation of hosts to begin with endosymbionts chosen from the generation before. This could take the form of vertical inheritance (in effect, perpetuating the walling in across generations), or else symbionts might be expelled to the external environment and reacquired by new hosts. In either case, it will be easier to evolve full cooperation from symbionts, enhancing the tendency towards miserliness in hosts.

V. DISCUSSION

A theme of recent work on symbiosis has been the surprising richness and complexity of the entanglement between host and symbiont, in which the partners undergo substantial metabolic and morphological changes mediated by a complex series of mutual signals, even modulating one another's gene expression [24]. It is clear that a model of the simplicity described here ignores many potentially relevant biological details. Its role is to show that, in principle, a low payoff by the host may be sufficient to coerce a population of endosymbionts into nearly complete cooperation. An assumption of both the theoretical analysis and the model is that the host is able to respond to individual symbionts, preferentially rewarding those who cooperate [25]. Perhaps the complexity of the real-life symbiotic dialogue concerns the host's efforts to detect and respond at a local scale to the efforts of its symbiont passengers. The punishment of defecting symbionts may not require the host to differentiate individual symbionts, however. Suppose, for example, that a host species is well served by symbionts that convert some compound X into some other compound Y. Even if the host is unable to reward the production of Y at a local scale, it can punish endosymbionts that do not carry out the reaction by flooding the area with something that is toxic to them in the presence of X, or toxic in the absence of Y. A mechanism like this potentially allows a single host to interact with an essentially arbitrary number of symbionts at the same time.

The theory proposed here accounts for both the persistence of host-endosymbiont mutualisms and the observed asymmetry in their benefits, as well as suggesting a role for the complex host structures now being found in many associations. The very different dynamics found in a two-species interaction, when compared with the usual iterated Prisoner's Dilemma, suggests that there is still much to be discovered about cooperative associations.

ACKNOWLEDGMENT

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