Evolutionary stability of host-endosymbiont mutualism is reduced by multi-infection

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Introduction

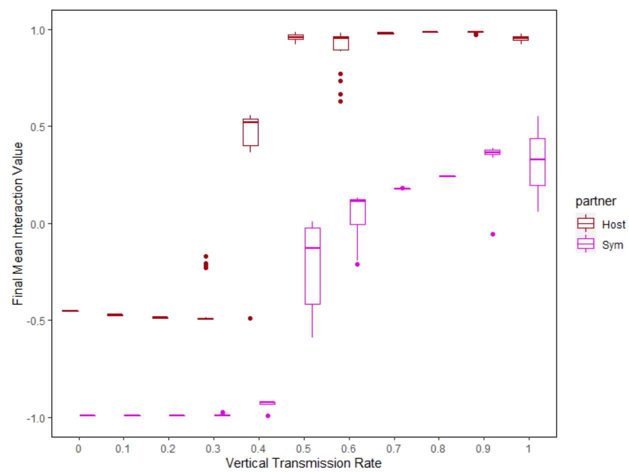
The human gut microbiome is a complex network of bacteria, phage, and other microorganisms, all interacting with each other in different ways. Many of these interactions occur between a host organism (such as a bacterium) and an endosymbiont (such as a phage) that lives inside it. These host-endosymbiont interactions range from mutualistic to parasitic. In a mutualistic interaction, the host and endosymbiont cooperate with each other and both benefit. In contrast, in a parasitic interaction the endosymbiont steals resources from the host and the host expends resources attempting to defend itself, so both suffer. Over the course of many generations, the behavior of hosts and endosymbionts can evolve.

A central evolutionary question in this context is whether hosts and endosymbionts will coevolve towards mutualism or antagonism. To date, evolutionary theory concerning this topic has focused on pairwise interactions (*i.e.* between a single host and endosymbiont). However, most hosts are home to vast numbers of endosymbionts, which co-evolve with each other just as they co-evolve with the host. The evolutionary consequences of this multi-level co-evolution are not well understood (but see (Nelson and May, 2017) for a preliminary mathematical modeling framework). Here we conduct initial inquiries into how existing host-symbiont co-evolution theory must change to accommodate the presence of multiple symbionts.

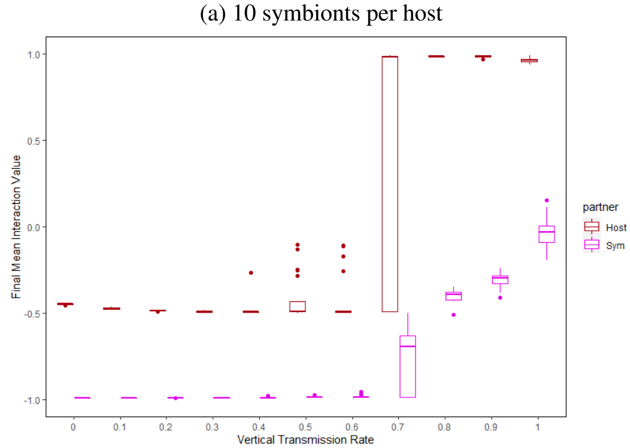
A factor that is known to be important in determining the course of pairwise host-symbiont co-evolution is vertical transmission rate: the probability of the endosymbiont's offspring ending up in the host's offspring as a result of the host's reproduction process. Prior research has shown that higher vertical transmission rates promote the evolutionary stability of mutualism (Vostinar and Ofria, 2019). However, it is unclear whether this relationship will persist when multiple endosymbionts are allowed to inhabit the same host.

Methods

We addressed this question using Symbulation, an agent based model of co-evolution between host organisms and symbionts, as a simple environment in which to observe the



(a) 10 symbionts per host



(b) 20 symbionts per host

Figure 1: **Evolved interaction values with 10 symbionts per host (top) and 20 symbionts per host (bottom).** Boxplots show distribution of evolved interaction values for hosts and symbionts across vertical transmission rates.

evolution of interactions between these organisms (Vostinar and Ofria, 2019). In Symbulation, the behavior of each individual is characterized by an "interaction value" between -1 (antagonistic) and 1 (mutualistic). This value determines the relationship between each organism and its partners, if it has any. At every time step, the host receives resources. Some of these resources may be passed on to its symbiont(s), based on the host's interaction value. Similarly, if the symbiont receives resources from the host, its interaction value determines whether it returns any resources back to its host. A highly antagonistic host will invest its resources into its own defense and not cooperate with the symbiont, while a highly cooperative host will donate some of its resources to its symbiont partner(s). When an individual accumulates enough resources, it reproduces. On reproduction, the offspring's interaction value is mutated by a value drawn from a normal distribution; thus, interactions evolve over time.

We conducted a series of experiments (n=20 per condition) in which we varied 1) the vertical transmission rate, and 2) the number of symbionts that were allowed to inhabit each host. In each experiment, we observed the final evolved interaction values for hosts and symbionts.

Results

Every increase in the number of symbionts per host led to a further increase in the level of vertical transmission required for mutualism to be an evolutionarily stable strategy. Figure 2 shows results for 10 symbionts per host and 20 symbionts per host, but the effect was consistent across the full range from 1 to 100 symbionts per host. After that point the effect largely saturated, with mutualism persisting at low levels only when the vertical transmission rate was 100%.

We hypothesize that this effect is driven by a dynamic in which parasites can be thought of as cheaters not only with respect to the host, but also with respect to the other symbionts. A mutualistic host is essentially a public good to its internal symbiont population. By parasitizing the host, a symbiont achieves short-term gain for itself at the long-term cost of dis-incentivizing host mutualism. If a host population is invaded by parasites, it will be incentivized to become antagonistic, even if this hurts any remaining mutualistic endosymbionts. These preliminary results highlight the potential for rich interactions among endosymbionts to play a critical role in the evolution of host-symbiont interactions.

References

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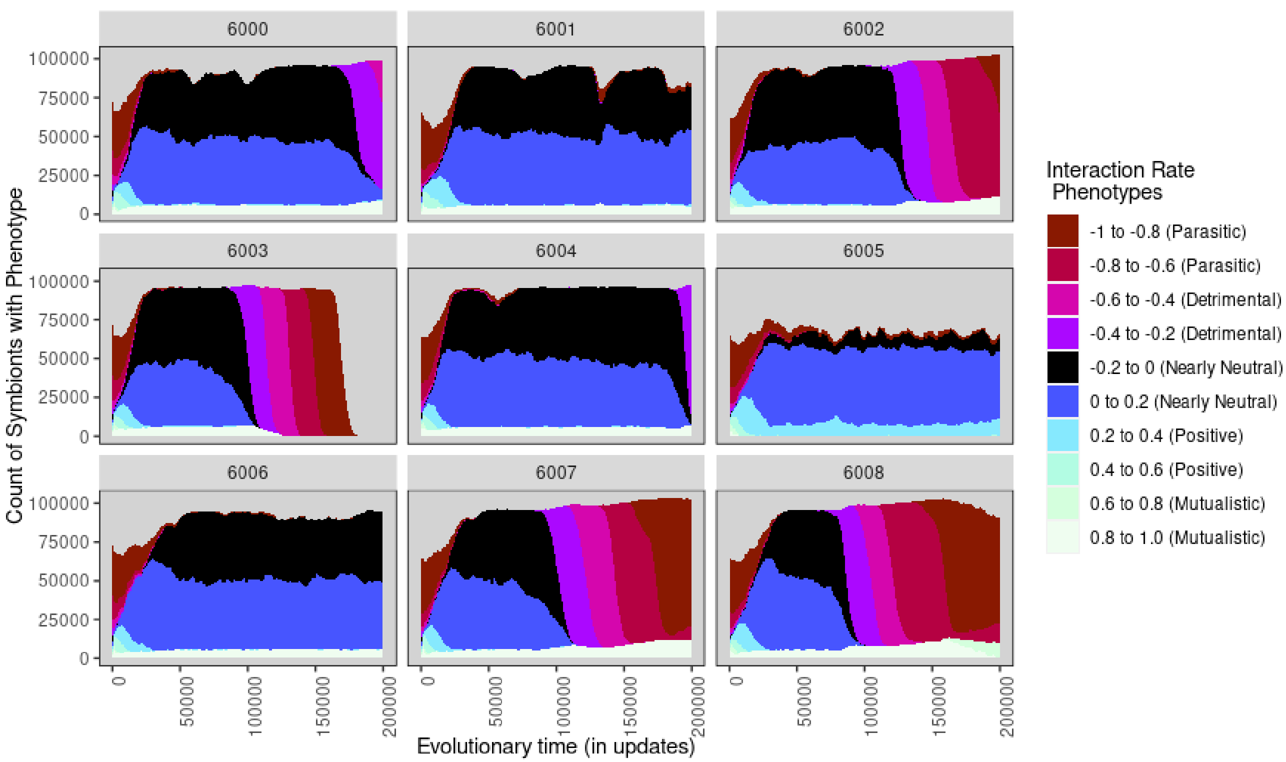

Figure 2: **Population dynamics of representative runs at vertical transmission rate of 60%.**