

NEWS AND COMMENTARY

Evolution of cooperation

The benefits of ridesharing

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Even the most primitive biological systems can evolve the means to mediate reproductive conflict, and a recent experiment has shown that we can watch it happen, in viral parasites.

Most of us enmeshed in the warp and woof of human social experience are acutely aware that the mediation of selfish conflict can be highly beneficial. Many other cooperative biological systems have learned this same lesson in an evolutionary sense by evolving behaviors that limit or negate reproductive conflict among individual units (Maynard Smith & Szathmáry, 1995; Sachs *et al.*, 2004). For example, conflict between most eucaryotic genes is eliminated by chromosomal linkage and fair meiosis that enforces proportional gene representation in gametes.

The experimenters Sachs and Bull (2005) designed a three-phase evolutionary cycle that, during two phases (encounter of host cells and growth of viruses within host lineages), favored cooperation between two bacteriophages (f1 and IKE), but during a third phase (viral reproduction) favored selfish competitiveness. These bacterial viruses were allowed to co-evolve for 50 complete passages through this selective regime. f1 and IKE do not kill their bacterial hosts, but are extruded through the cell wall without lysis. Importantly, the host was not allowed to evolve, but was killed off and replaced with a fresh population in each new cycle. After evolution, components of viral fitness were measured for each cycle phase. The viral lineages might have evolved greater cooperation with one another, greater conflict, or both.

To enforce cooperation, Sachs and Bull first marked f1 and IKE with distinct antibiotic-resistance genes and then made the presence of both viral types vital for the growth of bacterial cells. Antibiotic-sensitive bacteria were mixed with f1 and IKE during the encounter phase. They then treated cells with both respective antibiotics so that only bacteria that had been successfully infected by both f1 and IKE genomes could grow. During evolution, natural selection should

have favored mutations in either viral type that increased the probability of coinfection.

During the second phase favoring cooperation, Sachs and Bull grew cells carrying both f1 and IKE to high density overnight in the presence of both antibiotics, so all growing cells were coinfecting and the viruses were only transmitted vertically from mother to daughter. Viral coinfection generally hinders bacterial growth due to increased viral protein load and any negative effects of viral interactions. Distinct viruses forced to coevolve in the same host cells without the opportunity for new infections should evolve more cooperative interactions that favor faster growth by their host.

In the final phase of each cycle, viruses were allowed to reproduce in host cells that were grown for a short phase, then killed. During this phase, natural selection should favor conflict between f1 and IKE because there is competition for limited host resources. For example, a mutant of f1 might realize superior fitness by conflicting with IKE genotypes in the same cell and reducing the proportion of host resources available to IKE. Across all host cells, 'selfish' mutant genotypes of both viruses that perform well during this conflict phase will be more highly represented in the encounter phase of the next evolutionary cycle.

At the onset of this experiment, the relative strength of selection for enhanced cooperation *vs* conflict was unclear. For example, a potentially extreme outcome was that one viral lineage might evolve to both replicate faster and to actively hinder the replication of the other viral type. If these effects were large enough, the relative frequency of the inferior competitor during the encounter phase might have become so low that extinction of the whole population due to a lack of coinfection events became possible. At the opposite extreme, f1 and IKE might have evolved some means to eliminate the selective force favoring reproductive conflict.

Unsurprisingly, performance by both f1 and IKE had improved in all three

cycle phases after 50 passages. Coinfection rates during the encounter phase increased, as did host growth rate after infection and viral output per cell during viral reproduction. What was surprising, however, was the evolution of a novel relationship between f1 and IKE that both enforced cooperation during the encounter phase and greatly reduced selection favoring conflict during viral reproduction.

After host infection and viral genome replication follows the packaging of genomes into protein coats that carry the genetic material between infections. The ancestral f1 and IKE genomes produced distinct coat types and would only rarely copackage into the same coat. f1 and IKE solved the problem of increasing their coinfection rate in dramatic fashion by evolving to make copackaging very common. Since copackaged viruses carry both antibiotic-resistance markers in one protein coat, they have a large selective advantage during the encounter phase over separately packaged genomes that require two or more infection events per cell rather than one.

Copackaging not only became common but also became the dominant mode of coinfection. During evolution, the IKE genome lost several genes required for coat assembly and thus became obligately dependent on f1 coats for its transmission. (This genome reduction may have been largely responsible for improved host growth by reducing the viral protein load.) By the time that self-packaging IKE viruses went extinct (around cycle 40), copackaging had become so frequent that the majority of successful coinfections in the encounter phase came from copackaged genomes rather than simultaneous infections by separately packaged viruses.

The evolution of increased copackaging served not only as a cooperative strategy to increase coinfection rates. It also effectively eliminated the selective force favoring conflict during the viral reproduction phase. When copackaging is the primary mode of coinfection, both viruses benefit from roughly equal proportions of each viral type, because deviations from a 50:50 ratio result in a suboptimal number of copackaging events. This removes the advantage of selfish reproductive strategies that exists when most coinfections result from multiple infections of singly packaged genomes.

In the Sachs and Bull experiment, the evolution of enhanced cooperation

in one life-history phase (encounter) led to the mediation of conflict in a different phase (reproduction). By increasing the physical cotransmission of cooperating partners, their reproductive interests were coupled where they had previously been divided. It would be interesting to know whether multiple replicates of this same experiment would all generate the same con-

flict-mediation strategy or whether radically different outcomes would also occur. Physical coupling of evolutionary interests is a fundamental feature of many cooperative systems, and this study demonstrates the power of microbial systems to illuminate, in real time, evolutionary pathways leading to enhanced biological cooperation.

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