G
groups of cooperating organisms can obtain advantages in for-
gaging, predator defense, and environmental manipulation
that are impossible for individuals to achieve on their own. Although classically studied in the context of animals, co-
operation is now understood to be common among microscopic organisms ranging from viruses (1) to bacteria (2) to
unicellular eukaryotes (3). Every system of cooperative agents is potentially suscepti-
bile to cheating, and biologists have devoted tremendous effort to understanding how cooperation resists exploitation (4).
In PNAS, Waite and Shou (5) demonstrate that cooperation can avoid cheating by hitchhiking with beneficial mutations (6, 7).

Sophisticated systems of mutual helping, such as coordination among individuals of the slime mold Dictyostelium discoideum or mass cooperation within Hymenopteran insect colonies, are often protected from exploitation by antagonistic pleiotropy, privatization of public goods, conditional expression, or policing. However, how are relatively young, simple systems of cooperation stabilized if none of these or other supportive mechanisms, such as pop-
ulation spatial structure (8), are in place? Waite and Shou (5) offer a potential answer to this question.

The authors use three engineered strains of the yeast Saccharomyces cerevisiae to implement mutualism and cheating (9). Two of the strains are mutualists, including a lysine auxotroph that secretes adenine and an adenine auxo-

troph that secretes lysine; unless they are together, they cannot grow in minimal medium. The third, a cheater strain, is also a
lysine auxotroph and thus depends on the lysine secretor, but it does not provide anything in return. After documenting that the cheater strain has a fitness advantage because it does not pay the cost of secre-
ting adenine, the authors inoculate the three strains together at a 1:1:1 ratio in mixed liquid minimal medium. As a result of the cost of cooperation, the default prediction is that the cheater strain will gradually overtake the mutualists.

Something quite different occurs, however. Approximately half the replicates populations grow successfully in the mini-

mal medium, whereas the other half grow very slowly. The slowly growing populations consist mostly of dead cells, and the large majority of living cells are cheaters to scavenge lysine more quickly than competing cells.

**Mutualism and Evolutionary Dynamics**

Several notable observations follow from the work of Waite and Shou (5). Although the ability to hitchhike with beneficial mutations is certainly not unique to cooperative phenotypes, it may be especially important for cooperation. This is because the spread of an advantageous mutation also reduces genetic variability in the local patch, which is very good for the spread of cooperative phenotypes. The result is that local patches will tend to have cooperative phenotypes or cheater phenotypes, but not both. More formally, within-patch variance decreases while between-patch variance increases, increasing the relatedness coefficient associated with the social phenotype. This is exactly the condition that favors the evolution of cooperation, because it ensures that cooperators can work together rather than be exploited and overtaken by cheaters (10, 11).

It is especially fascinating that the two members of the lysine/adenine auxotroph mutualism have tightly linked evolutionary fates in competition with a cheating strain. When the mutualist competing with the cheater for lysine acquires a beneficial mutation for lysine uptake first, it gains a tremendous advantage, but it does not leave its mutualist partner behind upon riding its selective sweep. On the contrary, the adenine auxotroph joins in the sweep of the population by virtue of obligate interdependence between the two mutualists. The lysine auxotroph, although now superior to the cheater in lysine scavenging, still requires its lysine-secreting partner to grow. So, even though the selective sweep removes the genetic variability that is harmful to the evolution of cooperation—that between the cheater and its cooperator—it does not remove the genetic variability necessary for the mutualism to persist. The capacity of mutualist partners to hitchhike with each other will help to maintain diversity in microbial communities that contain mutually helping strains or species.

**Fig. 1.** Alternative outcomes for competition between two mutualists (A and B), and a cheating strain (C). The outcome of competition depends on whether the cheater acquires a beneficial mutation first or not. The cheater strain has a fitness advantage, but if it is not able to grow in the presence of the lysine/adenine auxotroph, it is outcompeted by the two mutualists. When the cheater strain acquires a beneficial mutation first, it gains the ability to grow and outcompetes the two mutualists. On the contrary, when the two mutualists acquire such a mutation, they gain the ability to grow and outcompete the cheater strain. The result is that cooperation resists exploitation (4).

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1To whom correspondence should be addressed. E-mail: cnadell@princeton.edu.

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**Importance of Ecology**

In addition to influencing the evolutionary fate of cooperation and mutualism, selective sweeps are predicted to affect the degree of genetic divergence among geographically separated populations, and thus to help determine the functional distinction between different microbial species (12). Experiments have documented selective sweeps in numerous microbes grown in the laboratory (13), and, although comparative genomics suggests the occurrence of sweeps in natural populations (14), we do not yet have an understanding of how often and how widely they occur in nature. In fact, recent work has challenged the importance of selective sweeps for the ecology of one set of Vibrio species (15). The magnitude and frequency of environmental disturbances are likely to be central, but these factors may vary dramatically from one bacterial species to another.

Spatial structure and heterogeneous strain distributions (i.e., deviations from well-mixed interactions within a patch) are common in cell groups and known to affect the speed and direction of selective sweeps and social evolution (16–18). Waite and Shou (5) perform their experiments in mixed liquid culture with strains of yeast that do not group together, deliberately avoiding the population spatial structure that can heavily influence the evolution of cooperation (19). This method was important for showing that cooperation can evolve by hitchhiking, but it would be interesting to see how the hitchhiking effect behaves in surface-bound microbial communities, where cells interact primarily with nearest neighbors (20).

In summary, Waite and Shou (5) show that the evolution of cooperative interactions may be supported simply by virtue of linkage with other traits under strong positive selection. Furthermore, obligate mutualists hitchhike with one another, even when only one partner in the mutualism possesses the gene that is selectively favored. It has also been suggested that hitchhiking may help to stabilize cooperation when it is in place, because cooperators will be more common and so more likely to acquire new beneficial mutations than cheaters (7). The relative impact of hitchhiking on cooperation, however, depends critically on a key unknown: how prevalent are selective sweeps among microbial species?