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Alternative Actions for Antibiotics
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To visualize this transition, the authors used spin- and angle-resolved photoemission spectroscopy to measure the spin and electron energy as a function of electron momentum. The replacement of S with Se creates metallic surface states with a linear energy-momentum relation. These surface extensions of the conduction and valence bands touch at a single node, called the Dirac point. The authors also observed subtle changes in the crystal lattice with x-ray scattering data. First-principles electronic structure calculations suggest that the transition depends on both the lattice changes and enhanced spin-orbit coupling.

Xu *et al*. take a further important step toward tuning the properties of the topological insulator by dosing a molecule, NO_2, on the surface that allows a tuning of the Fermi energy of the surface states. This step leads to a "texture inversion" of the spin-momentum relations when the Fermi energy passes through the Dirac point, as illustrated in the figure. Most of the novel electric and magnetic responses of topological insulators known to date rely on this tuning of the Fermi energy near the Dirac point (*7*, *8*). A theoretical proposal for a "topological excitonic condensate," an unusual symmetry-broken state with fractional charges (±e/2, where e is the charge of the electron) that could be formed by topological insulators, may also be a step closer with this new experimental technology (*9*).

Despite the experimental accomplishments reported by Xu *et al*., there are many challenges that remain if topological insulators are to become functional components of electronic devices. Chief among them are the problems of "aging"—the material properties degrade on a time scale of hours to days. Also, the bulk conductivity is unacceptably high and greater than what theory has predicted. However, there are good reasons to hope for substantial improvements in sample quality. The material Bi_2Te_2Se (where Tl is replaced by tellurium) was recently shown (*10*) to have a more insulating bulk, with up to 70% of the electrical conductance coming from the surface—more than two orders of magnitude better than most topological "insulators." Parallel methods of sample fabrication—chemical synthesis and molecular beam epitaxy—are expected to continue to lead to sample improvements in the near future.

Thus far, the known topological insulators are derived from materials with s- and p-type orbitals (which typically have weak electron correlations), and experiment has largely operated in the mode of confirming theoretical predictions. A new frontier with experimental surprises likely lies in the direction of more strongly correlated materials with d- and f-type electrons (*11*–*16*), which should expand the exciting choices already on the insulator menu.

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MICROBIOLOGY

Alternative Actions for Antibiotics

Compounds recognized as having antibiotic functions may have other possible roles in microbial interactions.

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Microbes generate signals, which coordinate mutually beneficial activities (*1*). They also produce antibiotics that kill prey, suppress competitors, or deter predators (*2*). Recent observations have led to the view that antibiotics often act as mutually beneficial signals (*3*–*6*). Exposure to sublethal concentrations of antibiotics can indeed alter microbial metabolism and even change behavior in beneficial ways, triggering reactions such as fleeing or hiding within the protective environment of a microbial aggregate (biofilm). But the weapon-signal dichotomy of functions for these compounds is a false one—there may be other possible information-related actions of naturally produced antibiotics: cues and manipulation.

The antibiotic-as-beneficial-signal hypothesis proposes that in nature, antibiotics evolved as a means of communication between unrelated species of microbes, but cause death in the laboratory as a result of unnaturally high cell densities and antibiotic concentrations (*4*–*6*). Evolutionary theory, however, predicts that bona fide signaling between different species will be rare (*7*). That is, if producing metabolically costly signaling molecules aids a recipient without preferentially benefiting the sender, then it is a form of altruism and is unlikely to persist evolutionarily. By contrast, individually costly signaling can evolve among relatives through kin selection, which favors the reproductive success of an organism's relatives, even at individual cost (*8*). However, altruism toward another species is more difficult to explain. Evolutionarily stable between-species signaling would require a shared interest, such that both sender and receiver benefit as a result of the communication. Such shared interests are rare among species competing for the same limited resources. Reflecting the stringent conditions required for its evolution, mutually beneficial signaling between animal species is much less common than signaling within species (*7*).

Beneficial signaling, however, is not the only possible alternative function for compounds with antibiotic (lethal) effects. Microbes detecting a low concentration of an antibiotic may interpret the compound as a cue that enables them to predict future exposures to an increased concentration. This cue allows them to respond in ways that reduce their susceptibility. For example, the bacterium *Pseudomonas aeruginosa* responds to sublethal concentrations of the antibiotic tetracycline by forming biofilms (*5*), thereby reducing future exposure to antibiotics (*9*), much as an animal joining a herd reduces its exposure to predation. Because joining a biofilm reduces the efficacy of the antibiotic, this action benefits the exposed microbe, with-

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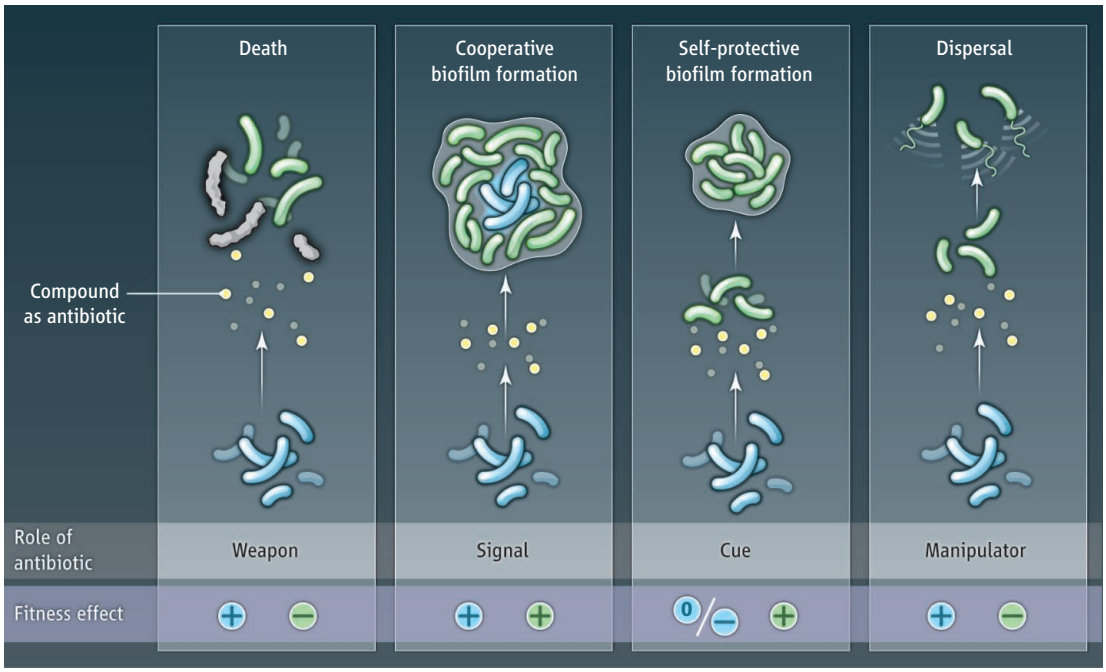

Naturally produced antibiotics. At high concentrations, microbially produced antibiotics can damage or kill other microbes. At low concentrations, these compounds can elicit changes in the behavior of other microbes. These alternative functions can be determined by examining the fitness consequence of producing the compound.

out preferentially benefiting the producer as would be required to qualify as a signal. Consistent with the hypothesis that antibiotics can act as cues, metabolic by-products generated by producer microbes, such as cell wall fragments and DNA, clearly not released to transmit information, can also induce behavioral changes that may benefit exposed recipient microbes (*10*).

It is also possible that compounds with antibiotic effects act as manipulating factors. For example, some microbes manipulate others by mimicking within-species signals used to coordinate group-level behaviors such as virulence, sporulation, or biofilm formation (*1*). This can trick the exposed microbes into adopting maladaptive physiological states or behaviors. For example, exposure to the antibiotic tobramycin causes *P. aeruginosa* to increase motility and flee (*5*). Consequently, competition for resources by the microbe that produces the antibiotic is reduced. Some acts of manipulation are quite sophisticated: Social amoebae in the genus *Dictyostelium* gather by the thousands when starved and cooperatively sporulate. *D. caveatum* has evolved to enter an aggregate of *D. discoideum*, produce a small molecule that inhibits sporulation, and then consume the thwarted *D. discoideum* (*11*). In this case, the small molecule does not function in a direct lethal manner; nor does it act as a signal because only the producer benefits from this communication. Moreover, manipulation is not limited to microbe-microbe interactions, but can cross biological domains. The nitrogen-fixing bacterium *Bradyrhizobium elkanii* produces rhizobitoxine, a chemical that inhibits its legume host's ability to make the hormone ethylene, reducing plant growth but increasing the bacterium's resource acquisition (*12*).

Whether a microbial compound acts as a weapon, signal, cue, or manipulator depends on the fitness consequences of the interaction (see the figure). Signals benefit both the sender and recipient, cues benefit the recipient but not the sender, and manipulation benefits the sender but hurts the recipient (*8*). Weapons, like manipulation, benefit the producer at the expense of the recipient, but accomplish this by causing death or injury instead of inducing maladaptive behavior. To determine the function of these compounds in nature, these fitness consequences must be measured in the environment in which the microbes evolved.

If microbes of many different species were altruists and in constant communication among each other for mutual benefit, then it would follow that antibiotics may act as "collective regulators of the homeostasis of microbial communities" (*5*). But this argument has little evolutionary merit: Heritable variation among communities is small relative to that within communities, partly because individuals migrate among communities. Individual and kin selection, therefore, swamp community-level selection, and individuals never evolve mechanisms for the benefit of the community as a whole (*13*). Similarly putative signals released by human gut microbes to mediate beneficial outcomes for both microbes and humans (*14*) may actually represent manipulation or inadvertent cues, respectively, depending on whether they decrease or increase the host's immune responses.

In examining the roles played by antibiotics, we should not ignore the possibility of multiple functions. Molecules classified as antibiotics may indeed be used as signals to coordinate behavior among related microbes. Research that unravels the specifics of this communication will improve our understanding of microbial evolution and ecology and may lead to new treatments for microbial infection. For example, bacterial biofilms are a major contributor to the persistence of microbial infections in humans. These may be treated by interfering with signals required to form biofilms (*15*) or by deliberately providing signals coordinating dispersal (*16*), both examples of human-mediated manipulation.

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