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Bacteria mix and mingle with microscopic fervor

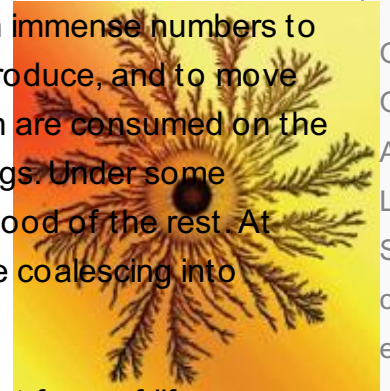
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Welcome to a vibrant social scene that has operated largely in secret until the past few years

Welcome to a vibrant social scene that has operated largely in secret until the past few years. Its participants don't seem to mind going unnoticed. They congregate in immense numbers to fend off enemies and the brute forces of nature, to obtain food, to reproduce, and to move to greener pastures. They're adept at forming bands to hunt prey, which are consumed on the spot. Vital messages repeatedly course through these assembled throngs. Under some circumstances, certain community members sacrifice their lives for the good of the rest. At other times, entire congregations cozy up to unsuspecting hosts before coalescing into stone-cold killers.



All this high drama occurs in the microscopic world of bacteria. As the first form of life on Earth, one-celled organisms have lots of experience in getting together by the billions or even trillions to procure and process energy sources. Yet only in the past several years have scientists with a variety of academic backgrounds launched an intensive effort to explore the social lives of bacteria and other microorganisms.

Research on bacterial gatherings got a boost in 2001 from behavioral ecologist Bernard J. Crespi of Simon Fraser University in Burnaby, British Columbia. Crespi reviewed findings from the past few decades on social behavior among microorganisms that "would be strangely familiar" to researchers who study the social ways of insects and vertebrates, he concluded.

Cooperation among individuals lies at the heart of social behavior in both microbes and animals visible to the naked eye, according to Crespi. For instance, just as bees build hives, many bacterial species create and inhabit sticky substances known as biofilms. Bacteria encased in biofilms thrive in moist settings, such as on ships' hulls, in sewage-treatment plants, on our teeth, and sometimes, with ill effects, in our lungs.

As in coalitions of creatures such as ants and naked mole rats, Crespi adds, bacterial colonies often feature a division of labor in which some members rarely or never reproduce but nonetheless provide other critical services to the community. *Rhizobium* bacteria, for example, form nodules that transfer nitrogen to plant roots and shuttle essential carbon to bacteria in and just outside the nodule. Bacteria in the nodule often refrain from reproducing, while their neighbors on the outside multiply fervently.

"The study of social behavior in bacteria has taken off in the last 3 or 4 years," says behavioral ecologist Ashleigh S. Griffin of the University of Edinburgh. "It's much easier to do experimental work on such behavior in microorganisms than in traditionally studied animals."

Scientists predict that understanding of bacterial cooperation and communication will yield medical breakthroughs. In particular, with such knowledge, researchers may devise new ways to undermine bacterial social bonds and thus neutralize virulent strains before they can kill a person.

Secretors and cheaters

Evolutionary theorists have held for more than 40 years that close genetic relations inspire cooperation. In a process known as kin selection, individuals help their relatives, who then spread copies of genes that the helpers also possess.

Nepotism of this sort frequently occurs in bacterial colonies, many of which consist of cells with identical DNA. However, genetic ties don't always bind. Cooperation in a group of bacteria crumbles when neighbors, even if they are close relatives, compete among themselves for critical resources, Griffin says.

In contrast, cooperation surges if neighbors sharing only weak genetic bonds compete with other genetically diverse groups for resources, she and her coworkers report in the Aug. 26 *Nature*.

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These results support the notion of group selection, an idea so controversial in evolutionary circles that Griffin declined to raise it by name in her paper. Group selection favors the spread of genetically linked traits that foster cooperation among individuals, even if those organisms are unrelated and some of them die as a result of their altruism.

Group-selection proponents have argued for the pattern that Griffin reports: Cooperation when different groups compete for common resources but not when competition occurs primarily among members of the same group.

David C. Queller of Rice University in Houston holds that group selection exerts a lesser influence on social behavior and evolution of microorganisms than kin selection does. However, Griffin's findings show that group selection as a testable theory has matured enough to be taken seriously, Queller says.

Griffin's team studied *Pseudomonas aeruginosa*, a bacterium that infects the lungs of people with cystic fibrosis. In communities of this microorganism, many cells respond to iron deficiency by secreting substances called siderophones. These compounds chemically vacuum up scarce iron and make it available both to secretors of siderophones and to any nearby microbes bearing a DNA mutation that blocks siderophone production.

These mutants, to put it bluntly, survive by sponging off their harder-working neighbors. Yet microbial cheaters of this ilk don't always prosper, Griffin finds.

In the laboratory, her group examined 12 *P. aeruginosa* communities at a time. The researchers then tracked those groups over ensuing generations. Conveniently, siderophones imbue secretors with a green tinge, as opposed to the white of cheaters.

Members of some groups were grown from a single bacterium and thus their members were almost identical genetically, and mainly secretors or cheaters. Other groups came from two bacteria, one secretor and one cheater, and thus exhibited a more even mix of secretors and cheaters.

The researchers then manipulated iron competition in the bacterial communities and looked for differences in evolution between the groups with almost-identical members and those with more-diverse members.

In one approach, the scientists mixed together the dozen groups and removed large numbers of microbes at random to initiate a new set of colonies. This random-selection process was repeated six times, in each instance after colonies had produced about seven generations of bacteria.

As the scientists suspected, colonies that collected more iron than others did also reproduced at a faster rate and contributed more individuals to the next randomly selected set of colonies.



In a second approach, the scientists removed an equal number of microbes from each of the original 12 bacterial colonies to establish new colonies. No mixing occurred among the colonies. This setup encouraged bacteria in each colony to compete among themselves for iron, irrespective of what neighboring communities did.

In line with kin selection, colonies with closely related members evolved larger numbers of cooperative secretors than colonies with more diversity did, regardless of the competitive arrangement.

Moreover, in closely and weakly related groups alike, competition that was limited to bacteria within each colony yielded more cheaters than did situations in which colonies competed against each other for survival.

In fact, competition within colonies left closely related groups with equal numbers of secretors and cheaters rather than a preponderance of secretors, a finding at odds with the traditional notion that kinship always generates lots of cooperation.

Competition among colonies produced the largest numbers of secretors, even in groups with weak genetic ties.

Disease-causing bacterial colonies may gain strength as they joust with each other in an infected host, Griffin theorizes. She is now collaborating with cystic fibrosis researchers to develop sneaky medical interventions that undermine these bacterial colonies. For example, Griffin and her coworkers would like to see whether substances that promote competition within *P. aeruginosa* colonies disrupt their cooperative iron foraging and so their infectious punch.

Genetic fair play

Recent studies have probed other varieties of bacterial teamwork. For example, in 2003, Gregory J. Velicer of the Max Planck Institute for Developmental Biology in Tübingen, Germany, exposed an innovative social tactic in *Myxococcus xanthus*. These soil-dwelling bacteria swarm over their microbial prey, breaking them down with enzymes and consuming them.

Velicer inactivated a gene in *M. xanthus* that regulates the growth of tiny structures on the cell surface. Scientists consider these structures crucial for group swarming. Colonies deprived of the gene's normal activity became stationary—for a while.

But within the next 9 months, the bacteria evolved a new way to move and began to swarm again. Colony members secreted unusually large amounts of a glue-like material that made clusters of *M. xanthus* literally stick together. The original swarming bacteria had produced smaller quantities of the glue.



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Another 2003 investigation, directed by evolutionary biologist Paul B. Rainey of the University of Auckland in New Zealand, focused on laboratory populations of *Pseudomonas fluorescens*, another infectious bacterium that causes illness.

When placed in a glass vial of broth, these microbes evolve into genetically distinct forms. Some colonize the container's floor, others stake out the rim, and a third group inhabits the broth's surface. Rainey calls this last group wrinkly spreaders because they produce a wrinkled layer.

Rainey found that colonies of wrinkly spreaders extract oxygen from the air and nutrients from the broth. Yet no single *P. fluorescens* bacterium could pull off this trick.

A critical genetic mutation enables wrinkly spreaders to produce a sticky biofilm that binds them into a mat that floats on the broth's surface, according to Rainey. Reproduction rates decline for individual bacteria that become wrinkly spreaders, but the survival advantages of group cooperation more than compensate for such a loss, he adds.

Cooperative microbial groups inevitably attract freeloading bacteria, such as the microbes that siphon off oxygen and nutrients from wrinkly spreaders without contributing any community-binding biofilm. Rainey plans to see whether wrinkly spreaders evolve systems for identifying and punishing, or perhaps destroying, cheaters.

Genes that foster social behavior play key roles in keeping cheating cells under control, report Queller and his coworkers in the Oct. 7 *Nature*. Genes that influence related traits evolve in ways that promote altruism while punishing selfishness, the researchers propose.

Queller's group studied cooperation not in bacteria but in slime mold colonies formed by cells of the social amoeba *Dictyostelium discoideum*. A shortage of its bacterial food causes a slime mold colony to form a fruiting body. In response to a chemical signal, some cells die to form a stalk that supports the other cells, which become reproductive spores.

The investigators created a mutant strain of *D. discoideum* that lacked a gene needed for recognizing the stalk-forming signal. Not surprisingly, when mixed into laboratory colonies deprived of food, members of this strain moved to the back of the structure, where spores develop. But in a startling finding, many fewer mutants ended up as spores than did the home strain of the organism. Thus, the mutants' ticket to the reproductive future didn't get punched.

Further tests suggested that some nonmutant cells tagged for stalk formation underwent a late developmental turnaround that primed them to replace genetic mutants that were about to become spores. The researchers don't yet know how the nonmutants bumped off the freeloaders.

The scientists suspect that many creatures, including bacteria, have evolved genetic means for penalizing those who leech off group efforts.

Micro messages

As bacteria gather in a colony, each individual bacterium needs to know when enough of its cohorts are present to make a biofilm or to carry out other communal duties. Members of many species of bacteria communicate that information by releasing hormonelike molecules that, after accumulating beyond certain concentrations, trigger a range of social activities. Scientists call this phenomenon quorum sensing.

More than 30 years ago, investigators first noted quorum sensing in two luminous bacteria, *Vibrio fischeri* and *Vibrio harveyi*. These seafaring bacteria inhabit organs that work like flashlights on the outside of some fish and squid. The microbes emit light when their populations reach a specific density.

Researchers today suspect that quorum sensing transforms various bacteria into infectious killers. For instance, virulent species may lie dormant in a host until they reach a critical density for releasing poisonous substances and resisting immune responses.

The signaling molecules used to coordinate quorum sensing come in two categories, according to microbiologist Bonnie L. Bassler of Princeton University. She and her colleagues find that one type of signaling molecule participates in chemical-communication systems that are unique to each bacterial species. Exclusive contacts within a species may be critical for distinguishing comrades from competitors in settings occupied by numerous bacterial strains, such as the human gut.

The second type of signaling molecule occurs in all bacteria and fosters communication across species, Bassler contends. Her investigations suggest that it activates genes that contribute to virulence as well as to swarming, biofilm formation, and some other social behaviors.

Research aimed at finding ways to disrupt these two signaling molecules could yield new treatments for bacterial diseases, the Princeton scientist says.

In a controversial take on such findings, physicist Eshel Ben Jacob of Tel Aviv University in Israel theorizes that bacteria exhibit fundamental forms of social intelligence that have traditionally been viewed as solely human. Continuously exchanged chemical messages within and among bacterial colonies impart meanings that change according to the situation, a basic facet of language, Ben Jacob and his coworkers argue in the August *Trends in Microbiology*.

Meaningful communication of this type fosters intentional behavior by bacteria, such as emitting and receiving pheromones in a courtship process before mating, Ben Jacob asserts.

Many researchers regard such ideas as a distraction from the job of understanding how bacteria communicate and what evolutionary forces have shaped their social behaviors.

Quorum sensing and other bacterial collaborations bear a general resemblance to social behaviors in other animals, remarks Velicer. "But I do not attribute intelligence to bacteria in any normal understanding of the term," he says.

However their behaviors are interpreted, it seems certain that bacteria will play out their lives under the gaze of a growing number of socially attuned scientists.

Citations

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Suggested Reading

Brownlee, C. 2004. Unhealthy change: Diversity in a bacterial colony can prolong infections. Science News 166(Nov. 20):324-325. Available to subscribers at [\[Go to\]](#).