The Secret Social Lives of Microorganisms

Like many organisms, microbes rely on both sociality and altruism to survive and flourish

Kevin R. Foster

As I stood there in the sweltering attic of an English pub, I remember asking myself "Why do I do this?"My face was a few centimeters from an unusually large hornet's nest, and things were about to get much worse. I tentatively put a bag around the brittle nest, but it fell from its moorings and exploded into a spray of hornets that immediately filled the attic. With a bee veil protecting me, I proceeded to collect the insects with my net, one by one. But growing impatient, I swung wildly and managed to shatter the bulb that hung from the center of the room. I was left standing in total darkness, covered in angry hornets.

The reason I was there is that hornets are not only strikingly beautiful creatures (when observed under better conditions) but are also an amazing product of social evolution. Like many bees and ants, their highly organized societies contain a single queen and a small army of specialized workers that ferociously defend and tend the young. What is remarkable is that many of these workers will never reproduce. Any reading of Darwin immediately reveals a problem here: why would natural selection favor an organism that gives up its own reproduction?

Darwin himself saw this difficulty and devoted a section of the *Origin* to the problem of worker sterility and the associated issue of how, once sterile, an individual could be subject to natural selection at all (if you do not reproduce, how can your traits be modified down generations into a specialized worker caste?). The answer of course is family life. Helping to raise your brothers and sisters—to whom you are genetically similar—is a perfectly good way to pass on copies of your genes. Familial gene sharing is so powerful that it can lead to the extreme case of the insect worker who labors her whole life without laying a single egg. The social insects have certainly earned the "social" in their name, and many biologists go even further, calling their selfless acts "altruistic" by analogy with human giving. But how far does this analogy go, and indeed can we take it further to the smallest of organisms? It was this question that led me, after my Ph.D., to move from insects to the world of microbes. I hope to convince you that, in important ways, microorganisms are altruistic too.

This idea seems ridiculous to some and, of course, there is no sense in which a microorganism ever displays the good intentions that often characterize human altruism. There is no cognitive root to their miniature gifts and exchanges. Nevertheless, the notion of the altruistic microorganism has a surprisingly long history, almost as long as the concept of natural selection. Herbert Spencer, a contemporary of Darwin, is widely credited with introducing and popularizing the term altruism in Victorian Britain alongside the term's probable inventor, Auguste Comte.

Spencer was a powerful intellectual figure who strongly promoted the importance of competition and evolution in human society through his catch phrase "survival of the fittest." Spencer used microbes in his discussions of social evolution and, moreover, suggested that there were important ways in which single cells were altruistic.

But I should not get ahead of myself. Before evaluating the idea of altruism, I will first consider the more general case for sociality in microbes. Is there any sense in which a bacterium has a social life? This idea too has been long aired. A particularly clear statement comes from Prince Kropotkin, a Russian anarchist who made several epic journeys into 19th-century

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Siberia. Amid the extreme cold and harsh conditions, he was struck by the importance of social interactions and, in particular, mutual aid among species. Kropotkin used these observations to bolster his argument for a decentralized and communist Russia. But it was his prediction that ‘‘we must be prepared to learn some day, from the students of microscopical pond-life, facts of unconscious mutual support, even from the life of microorganisms,’’ that has had more lasting success.

Kropotkin’s prediction, however, has taken time to reach the limelight. Modern microbiology rests upon the technique of vigorously shaking cells in liquid broth. This is ideal for many microbes; a washing-machine world where nutrients and oxygen are plentiful, a world where generations of microbiologists have studied the genetics and behavior of their favorite species. But the considerable benefit of growing cells in liquid can come at the cost of conceptual bias. The natural tendency for scientists is to picture species as single cells in a broth sea, where interaction is both rare and fleeting. This is at least partly correct. Many microbes, including the myriad that are found in marine plankton, do spend much of their lives swimming. One mode of swimming is the tail-like flagella of bacteria that spin rapidly and propel cells forwards; a telling example of how biology invented both wheels and motors billions of years before us. Flagella teach us that microbes are well adapted to a life in suspension, but there is another side to microbes that we were slower to recognize: a life in society.

We now know that much of what microbes do they do in dense groups of millions. Many bacteria like to stick themselves to surfaces where they can readily proliferate and, while doing so, encase themselves in sticky or slimy substances. These gatherings, known as biofilms, are found in all manner of environments. One such environment is your teeth, where millions of cells of many species are currently growing as incipient plaque. Biofilms will form on almost any surface, including those deep inside our bodies, upon medical devices, ship hulls, and food-processing equipment. The problem is compounded by the fact that biofilms can be tough and confer considerable antibiotic resistance on their inhabitants, making them difficult to remove. On the flip side, some such communities are vital for our health and well-being, including the microbial communities that clean our water in treatment plants and the massive numbers of bacteria that line our gut. An understandably favorite factoid of the microbiologist is that the bacteria within us outnumber our own cells by 10 to 1.

Everything that a cell does within a biofilm can have immediate consequences for its neighbors. This includes the most fundamental action of any microbe: cell division. Not only does division push others aside, it requires many resources that can be scarce in a densely packed group. The act of cell division is thus the act of taking food from others. Accordingly—as for a rebel reproducing worker in a hornet nest—natural selection can favor cells that divide as rapidly as possible in order to acquire as great a share of the resources as is possible. Recent events in both the economy and the environment reveal the human analogies to this situation. If left unchecked and unregulated, competition within any society has the potential to waste—and eventually ruin—shared resources.

This idea was summarized in a famous essay by the ecologist Garret Hardin. Hardin built his argument upon a story of a commons pasture in rural England shared by multiple herders. He observed that the best way for a herder to maximize their productivity is to keep adding cattle to graze, even though this threatens the pasture’s demise. This curious situation arises because, with a shared resource, all the benefit of adding a cow goes to the owner, while the cost to the pasture is shared among all herdsmen. From here, Hardin argued strongly—and controversially—that we need to find ways to regulate human population growth in order to avert environmental tragedy, an argument that may be more likely to be heeded now than it was originally.

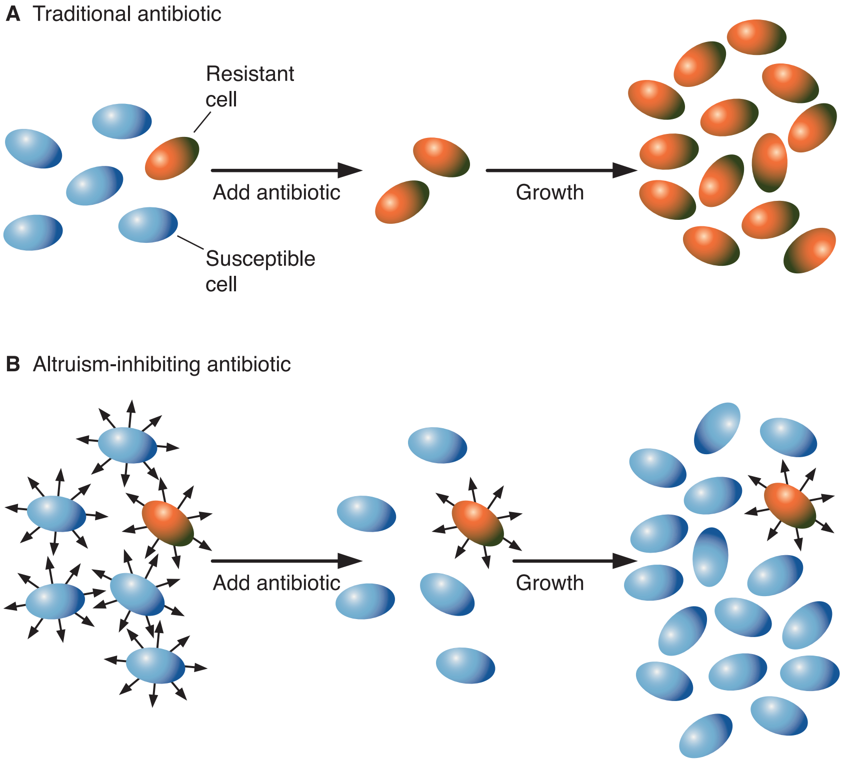
The potential for Hardin’s “tragedy of the commons,” is a problem shared by microbe and human alike. Natural selection can favor microbes that divide as rapidly as possible in order to maximize their short term gain, irrespective of the negative effects on others. Conversely, if a cell holds back on division and increases the total yield of a biofilm, the cell is displaying behavior that will have a positive effect on others. In this simple sense, a microbe can be said to be altruistic. Cells have the potential to display behaviors that slow their own reproduction and promote that of others. But why would a cell ever do this? Here, as for social insects, the key is again likely to be family life. As bacteria divide in a packed biofilm, they produce near-identical copies of themselves. This can create large clonal groups with a common evolutionary interest, even if the biofilm as a whole contains many competing strains and species. Consistent with the notion of altruistic behavior within biofilms, many microbial species are now known to secrete products that are costly in the short term but improve overall growth. These products include enzymes that break down food sources to a manageable size and scavenging molecules that help collect scarce resources, such as iron. Because the products are released into the environment, they are a shared resource and the secretions of any one cell will benefit many others around it.

Altruism is only beneficial if there are other cells around to receive the benefits. If a cell were to sit alone and secrete a growth promoting compound, there would be little benefit to anyone, as most of the compound would diffuse away and be lost. Microbes have evolved to deal with this problem by secreting cheaper compounds that are used to detect cell density (and possibly diffusion conditions). When these indicators reach a high enough concentration, the cells can sense that there must be many other cells around, and the conditions are ripe for secreting the more costly products.

This clever trick is of course quorum sensing. An effective society of microbes thus requires several of the key features of any prosperous society. This includes the need for individuals to perform selfless acts and the need for coordination that ensures these acts are well directed. The analogies to other societies is also illustrated by the potential for mutants that use the secretions of others without themselves contributing to the shared pool. This "microbial cheating" occurs both at the level of quorum sensing—where one strain of bacteria will use a quorum sensing signal without producing it—and also at the level of the many secretion systems that provide nutrients for growing cells. The emergence of such strains tends to decrease the growth rate of microbial groups.

What can be very bad for a biofilm, however, can be very good for us. Many pathogens rely on both quorum sensing and secreted products to inflict harm upon us. This includes the secretion of enzymes that kill host tissue by *Salmonella enterica* (typhoid fever) and *Pseu-domonas aeruginosa*; toxin production by *Bacillus anthracis* (anthrax) and *Vibrio cholerae*; and the widespread production of compounds that breakdown antibiotics, such as the β-lactamase enzymes that destroy penicillin.

The efforts of bacteria to cause infection and break down antibiotics often require them to act altruistically to one another. Curiously, our efforts to combat bacterial infections may also rest on altruism in our own societies. Antibiotics have a limited efficacy because bacteria nearly always evolve a way to become resistant, testament to what has become known as Orgel's second rule: "Evolution is cleverer than you are" (named after the biochemist Leslie Orgel). The more we use a given antibiotic, the sooner it becomes useless. As such, the diminishing pool of effective antibiotics represents a valuable societal resource for which a tragedy of the com-



The evolution of antibiotic resistance in a typical antibiotic (A) and a hypothetical antibiotic that targets a secretion, where the secretion is energetically costly to individual cells but promotes growth of nearby cells (B). In the conventional case, the resistant mutants rapidly outcompete the susceptible cells. In the latter case, resistant mutants that secrete have the potential to be outcompeted by susceptible cells that do not, because the susceptible cells can use the growth promoting secretion without paying the cost.

mons is worryingly imminent. The threat of a return to the horrors of the pre-antibiotic era of medicine may only be prevented if patients with mild infections altruistically forgo treatment for the greater good.

Or is there another way? Rather than focusing on antibiotic use within our societies, we might instead focus on microbial societies and the potential for their own micro-tragedies (Fig. 1). Traditional antibiotics act by killing or stopping cell division, and resistant mutants, that can grow in the presence of the antibiotic rapidly replace the original susceptible strains. Consider instead a drug that attacks a cell's ability to secrete an altruistic compound that is needed for growth. Resistant mutants that re-evolve secretion will promote the growth of susceptible cells around them. And, more than this, the susceptible cells do not pay the cost of secretion, which can put the resistant strain at a competitive disadvantage. At least in principle, this can slow the rise of antibiotic resistance. By recognizing that microbes rely on both sociality and altruism to cause infection, a novel strategy for treatment is revealed.

SUGGESTED READING

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