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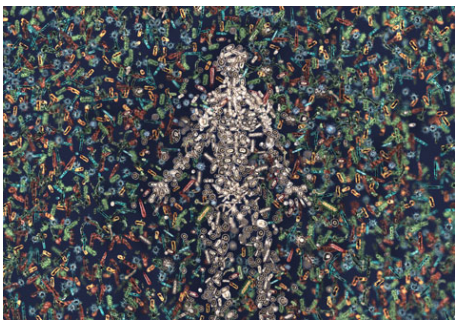
# Bacteria 'R' Us

**Emerging research shows that bacteria have powers to engineer the environment, to communicate and to affect human well-being. They may even think.**

By Valerie Brown





*(Illustration by Bryan Christie)*

*Today's revelation in the journal* Science *that researchers have found a bacterium in California's Mono Lake that can thrive on arsenic — usually implicated in killing life, not sustaining it — is quickly revolutionizing our conception of what is life and where it might be found. To help in deciphering the direct contribution bacteria make to human life, we're reposting this story which originally debuted on Oct. 18.*

A few scientists noticed in the late 1960s that the marine bacteria *Vibrio fischeri* appeared to coordinate among themselves the production of chemicals that produced bioluminescence, waiting until a certain number of them were in the neighborhood before firing up their light-making machinery. This behavior was eventually dubbed "quorum sensing." It was one of the first in what has turned out to be a long list of ways in which bacteria talk to each other and to other organisms.

Some populations of *V. fischeri* put this skill to a remarkable use: They live in the light-sensing organs of the bobtail squid. This squid, a charming nocturnal denizen of shallow Hawaiian waters, relies on *V. fischeri* to calculate the light shining from above and emit exactly the same amount of light downward, masking the squid from being seen by predators swimming beneath them.

For their lighting services, *V. fischeri* get a protected environment rich in essential nutrients. Each dawn, the squid evict all their *V. fischeri* to prevent overpopulation. During the day, the bacteria recolonize the light-sensing organ and detect a fresh quorum, once again ready to camouflage the squid by night.

This tale of bobtail squid would be just another mildly jaw-dropping story in a natural world full of marvels if it weren't a portal into an unsuspected realm that has profound consequences for human beings. Regardless of the scale at which we explore the biosphere — whether we delve into the global ocean or the internal seas of individual organisms — bacteria are now known to be larger players than humans ever imagined.

Strictly by the numbers, the vast majority — estimated by many scientists at 90 percent — of the cells in what you think of as your body are actually bacteria, not human cells. The number of bacterial species in the human gut is estimated to be about 40,000, according to Daniel Frank and Norman Pace, writing in the January 2008 *Current Opinion in Gastroenterology*. The total number of individual bacterial cells in the gut is projected to be on the order of 100 trillion, according to Xing Yang and colleagues at the Shanghai Center for Bioinformation Technology, reporting in the June 2009 issue of *PLoS One*, a peer-reviewed online science journal. Xing calculated a ballpark figure for the number of unique bacterial genes in a human gut at about 9 million.

In fact, most of the life on the planet is probably composed of bacteria. They have been found making a living in Cretaceous-era sediments below the bottom of the ocean and in ice-covered Antarctic lakes, inside volcanoes, miles high in the atmosphere, teeming in the oceans — and within every other life-form on Earth.

These facts by themselves may trigger existential shock: People are partly made of pond scum. But beyond that psychic trauma, a new and astonishing vista unfolds. In a series of recent findings, researchers describe bacteria that communicate in sophisticated ways, take concerted action, influence human physiology, alter human thinking and work together to bioengineer the environment. These findings may foreshadow new medical procedures that encourage bacterial participation in human health. They clearly set out a new understanding of the way in which life has developed on Earth to date, and of the power microbes have to regulate both the global environment and the internal environment of the human beings they inhabit and influence so profoundly.

There's such ferment afoot in microbiology today that even the classification of the primary domains of life and the relationships among those

domains are subjects of disagreement. For the purposes of this article, we'll focus on the fundamental difference between two major types of life-forms: those that have a cell wall but few or no internal subdivisions, and those that possess cells containing a nucleus, mitochondria, chloroplasts and other smaller substructures, or organelles. The former life-forms — often termed prokaryotes — include bacteria and the most ancient of Earth's life-forms, the archaea. (Until the 1970s, archaea and bacteria were classed together, but the chemistry of archaean cell walls and other features are quite different from bacteria, enabling them to live in extreme environments such as Yellowstone's mud pots and hyperacidic mine tailings.) Everything but archaea and bacteria, from plants and animals to fungi and malaria parasites, is classified as a eukaryote.

Science has determined that life arose and became complex through a process generally known as evolution, but biologists are engaged in an energetic debate about the form of that evolution. In essence, the argument centers on whether the biosphere should be characterized as a tree of life or an interactive web. In the tree construct, every living thing springs from a common ancestor, organisms evolve slowly by means of random mutations, and genes are passed on from parent to offspring (that is to say, vertically). The farther away from the common ancestor, generally speaking, the more complex the life-form, with humans at the apex of complexity.

The tree-of-life notion remains a reasonable fit for the eukaryotes, but emerging knowledge about bacteria suggests that the micro-biosphere is much more like a web, with information of all kinds, including genes, traveling in all directions simultaneously. Microbes also appear to take a much more active role in their own evolution than the so-called "higher" animals. This flies in the face of the more radical versions of Darwinism, which posit that the environment, and nothing else, selects genes, and that there is no intelligence, divine or otherwise, behind evolution — especially not in the form of organisms themselves making intentional changes to their heritable scaffolding. To suggest that organisms as primitive as bacteria are capable of controlling their own evolution is obviously silly.

Isn't it?

In terms of the pace of evolutionary change, one advantage the single-celled have over complex organisms is reproductive speed. Unlike eukaryotes, bacteria usually reproduce by cloning, which simply copies the single parent's entire set of genes. If conditions are favorable, a population of bacteria can double every 20 minutes or so.

Achieving genetic diversity is a whole different thing. Most eukaryotes engage in sex, which combines reproduction with genetic mixing. This produces offspring carrying half of each parent's genes. But bacteria don't have sex, they transfer genes among themselves horizontally — and they do a lot of transferring. The primary method most bacteria use is called "conjugation," a process in which genetic material is transferred between two bacteria that are in contact. It's as close as they come to sex (although, as far as we know, lacking the romance; it's more like downloading handy little apps from a cool website). In principle, every bacterium can exchange genes with every other bacterium on the planet. A side effect of this reality: The notion of separate bacterial species is somewhat shaky, although the term is still in use for lack of a better alternative.

And bacteria don't just get together for "file sharing." Even before quorum sensing was discovered in *V. fischeri*, scientists had noted many examples of coordinated action, such as "swarming," in which a colony of bacteria moves as a unit across a surface, and the development of "fruiting bodies," in which bacteria glom together to form inert spores as a means of surviving severe environmental conditions. Since the dominant paradigm assumed that bacteria were dumb, discrete individuals, these phenomena tended to be glossed over until *Vibrio*'s highly sophisticated census-taking focused new attention on coordinated bacterial behavior. Group behavior has now been demonstrated so widely that many microbiologists view bacteria as multicellular organisms, much of whose activity — from gene swapping to swarming to biofilm construction — is mediated by a wide variety of chemical communications.

Bacteria use chemicals to talk to each other and to nonbacterial cells as well. These exchanges work much as human language does, says Herbert Levine of the University of California, San Diego's Center for Theoretical Biological Physics. With colleagues from Tel Aviv University, Levine proposed in the August 2004 *Trends in Microbiology* that bacteria "maintain linguistic communication," enabling them to engage in intentional behavior both singly and in groups. In other words, they have "social intelligence."

Bacteria can live solitary lives, of course, but they prefer to aggregate in biofilms, also known as "slime cities." Biofilms usually form on a surface, whether it's the inner lining of the intestines or inside water pipes or on your teeth. In these close-knit colonies, bacteria coordinate group production of a slimy translucent coating and fibers called "curli" and "pili" that attach the colony to something else. Biofilms can harbor multiple types of bacteria as well as fungi and protists (microscopic eukaryotes). A complex vascular system for transporting nutrients and chemical signals through a biofilm may also develop. As Tim Friend described in his book *The Third Domain*, explorers diving to the wreck of the *Titanic* found these features in "rusticles" — draped colonies of microbes — feeding on the iron in the *Titanic*'s hull and skeleton, more than 2 miles under the surface.

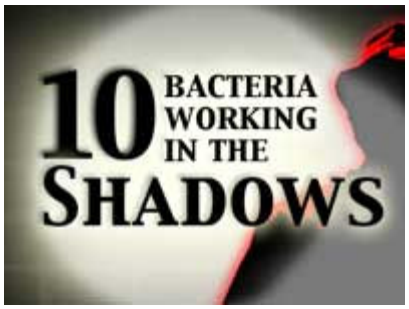
The abilities of bacteria are interesting to understand in their own right, and knowing how bacteria function in the biosphere may lead to new sources of energy or ways to degrade toxic chemicals, for example. But emerging evidence on the role of bacteria in human physiology brings the wonder and promise — and the hazards of misunderstanding them — up close and personal.

Because in a very real sense, bacteria are us.

In 2007, the National Institutes of Health began an ambitious program called the Human Microbiome Project, which aims to take a census of all the microorganisms that normally live in and on the human body. Most of these live in the digestive tract, but researchers have also discovered unique populations adapted to the inside of the elbow and the back of the knee. Even the left and right hands have their own distinct biota, and the microbiomes of men and women differ. The import of this distribution of microorganisms is unclear, but its existence reinforces the notion that humans should start thinking of themselves as ecosystems, rather than discrete individuals.

As of early 2010, the Human Microbiome Project had collected samples of microbial DNA from about 300 people and had sequenced or prepared to sequence the genomes of about 500 bacterial strains from these samples. Fifteen studies of microbial involvement in human disease have been funded. "These sorts of trials take time," says Microbiome Project program director Susan Garges, so clinical treatments based on the research from the project could be years off unless, she says, "in the shorter term, specific microorganisms are associated with a disease state." In that case, protocols for clinical diagnosis and treatment might be accelerated.

But the microbiome project is not just about disease-causing microbes such as *E. coli* and *Staphylococcus* strains. Many of the organisms it is identifying are responsible for regulating the digestive tract and keeping humans healthy in a variety of ways.




As Valerie Brown has shown, bacteria are indeed us. But who are these microscopic allies and enemies? Click this image to meet our Top Ten Bacteria Working in the Shadows.

The human gut is filled with large numbers of a wide variety of bacteria; clearly those that cause disease must rank high on the priority list of those to be studied, but the picture emerging from new research is that pathogens and beneficial bacteria are not necessarily mutually exclusive organisms. A microbe's effects on the human body can depend on conditions. And if you approach the human body as an ecosystem, some researchers are finding, it may be possible to tune that system and prevent many diseases — from acute infections to chronic debilitating conditions — and even to foster mental health, through bacteria.

Recent research has shown that gut microbes control or influence nutrient supply to the human host, the development of mature intestinal cells and blood vessels, the stimulation and maturation of the immune system, and blood levels of lipids such as cholesterol. They are, therefore, intimately involved in the bodily functions that tend to be out of kilter in modern society: metabolism, cardiovascular processes and defense against disease. Many researchers are coming to view such diseases as manifestations of imbalance in the ecology of the microbes inhabiting the human body. If further evidence bears this out, medicine is about to undergo a profound paradigm shift, and medical treatment could regularly involve kindness to microbes.

Still, in practice, the medical notion of friendly microbes has yet to extend much past the idea that eating yogurt is good for you. For most doctors and medical microbiologists, microbes are enemies in a permanent war. Medicine certainly has good reason to view microbes as dangerous, since the germ theory of disease and the subsequent development of antibiotics are two of medical science's greatest accomplishments.

But there's a problem: The paradigm isn't working very well anymore. Not only are bacteria becoming antibiotic-resistant, but antibiotics are creating other problems. Approximately 25 percent of people treated with antibiotics for an infection develop diarrhea. Moreover, people who contract infections just by being hospitalized are at risk of developing chronic infections in the form of biofilms. These not only gum up the works of devices such as IV tubes, stents and catheters, but also protect their constituent microbes from antibiotics.

In addition to antibiotic-resistant *E. coli* and *Salmonella* that often spread through our food supply, common pathogens that make doctors' blood run cold include *Pseudomonas aeruginosa* and *Clostridium difficile*. *P. aeruginosa* is responsible for about 40 percent of all fatalities from hospital-acquired infections. *C. difficile* is the culprit in at least a quarter of diarrhea cases caused by antibiotics. A 2007 study by the Los Angeles County Department of Public Health found that mortality rates from *C. difficile* infections in the United States quadrupled between 1999 and 2004. *C. difficile* will invade an antibiotic-cleansed colon and "poke holes in it," says Vincent Young, a gastrointestinal infection specialist at the University of Michigan. Some people in this situation rush to the bathroom 20 times a day. "It's not just an inconvenience," Young says.

Many researchers are focusing on inflammatory bowel disorders to understand how the balance between the intestinal microbes and their human hosts becomes deranged. Incidence of these diseases has sharply increased since about the mid-20th century, just about the time the industrialized world started eating highly processed foods and antibiotics came into widespread use. For example, in bowel disorders such as Crohn's disease and ulcerative colitis, excessive inflammation leads to severe pain, diarrhea and vulnerability to opportunistic germs. Standard treatments include powerful steroids like prednisone, surgical removal of the colon and heavy treatment with antibiotics.

But a more ecological approach is beginning to offer hope. *P. aeruginosa* and *C. difficile* are common residents of human bodies and under normal circumstances are benign. So what turns them into enemies? Most of the time, says John Alverdy, an intestinal and critical-care surgeon at the University of Chicago, bacteria "have to have a reason to hurt you." Surgery is just such a reason. A surgical patient's normal metabolism is altered; usually nutrients are provided intravenously instead of through the digestive system, so in a patient being fed by an IV drip, the gut bacteria perceive their sustenance disappearing. A decline in available nutrients alarms them. And surgery triggers the release of stress compounds that bacteria also sense, Alverdy says. Chemotherapy and radiation have similar effects. When threatened, bacteria become defensive, often

producing toxins that make the host even sicker. They also tend to speed up their acquisition of and purging of genes when under external selection pressure, of which antibiotics are an obvious and powerful example.

Alverdy is finding success in treating patients with a strategy he calls "ecologic neutrality." In research reported in the August 2008 *Surgery*, he was able to prevent *P. aeruginosa* from turning virulent in surgically stressed mice by dosing them with polyethylene glycol, which supplies the bacteria with phosphate, one of their primary needs. "Once they sense there's plenty of phosphate," he says, "they figure everybody must be happy here." The treated mice in his experiments, unlike the controls, did not contract fatal infections.

Some researchers are even exploring the idea of stool transplants — that is, introducing a healthy person's gut bacteria into a sick person's intestines via the donor's feces. Although there are not many peer-reviewed studies of this rather disturbing concept, a review in the July 2004 *Journal of Clinical Gastroenterology* by Australian researcher Thomas Borody found that in a large majority of the cases reported in the medical literature, fecal transplants resulted in almost immediate and long-lasting relief for people suffering from inflammatory bowel conditions and for those with chronic antibiotic-induced diarrhea. (There's definitely a market for fecal transplants. When one scientist mentioned the success of the procedure in an interview with *The Wall Street Journal*, he was inundated with calls from desperate patients begging for the treatment, even though he does not practice the therapy.)

If new therapies based on human microbial ecology just lessened antibiotic resistance and relieved the suffering of people with intestinal disorders, they would constitute miraculous advances. But the intensifying focus on the role of bacteria in human health is turning up other possible avenues for improving health.

Gut bacteria play a role in obesity, which affects about a third of American adults. The gut bacteria populations of the obese are less diverse than those of normal-weight people. Researchers have found that children whose fecal bacteria are composed more of *Staphylococcus aureus* than *Bifidobacteria* at birth are more likely to become overweight later in life. Interestingly, one study found that the microbiota of obese adults were very different from the bacteria populations of both normal-weight people and obese people who had had gastric bypass surgery. Researchers from Arizona State University and the Mayo Clinic noted that in obese people, there appeared to be a cooperative relationship between hydrogen-producing bacteria and the one archaean resident of the human gut, a hydrogen-consuming, methane-producing organism. The archaean partner makes fermentation of indigestible polysaccharides (which are complex carbohydrates) more efficient, and the extra fermentation products are converted to fat by the intestines. It appears that obese people's gut microbes are just too good at their jobs.

Research in animals supports the idea that gut bacteria play a role in weight regulation. According to recent research by Emory University pathologist Andrew Gewirtz and his colleagues, mice bred without a gene that allows them to detect the presence of gut bacteria unexpectedly became overweight and suffered from high blood pressure, high triglycerides and high cholesterol. When given access to a high-fat diet, they developed full-blown diabetes. Fecal transplants from these mice to normal mice transferred the health problems.

Despite these fascinating hints, scientists don't yet know whether changes in microbial equilibrium are the chicken or the egg — that is, whether they cause or are caused by obesity — making it unclear whether restoring a proper gut ecosystem can become a magic bullet to fire against obesity.

Researchers have found several reasons to believe that bacteria affect the mental health of humans. For one thing, bacteria produce some of the same types of neurotransmitters that regulate the function of the human brain. The human intestine contains a network of neurons, and the gut network routinely communicates with the brain. Gut bacteria affect that communication. "The bugs are talking to each other, and they're talking to their host, and their host talks back," Young says. The phrase "gut feeling" is probably, literally true.

For example, it's been known for a while that sick people get depressed and anxious. This seems so obvious as to be a no-brainer, but research suggests that some of the fear and fatigue associated with infections stems from immune responses affecting the brain.

Mark Lyte of the Texas Tech University School of Pharmacy noticed that lab mice dosed with *Campylobacter jejuni*, bacteria that are commonly a cause of food poisoning, were more anxious than control mice. After several experiments, Lyte's team concluded that the vagus nerve, which extends into the colon, was probably transmitting the news of a gut infection to the brain areas involved in emotions. Reporting their results in the August 2007 *Brain, Behavior and Immunity*, the team also conjectured that the anxiety often exhibited by victims of bowel disorders may operate on the same network, which is not under conscious control.

Even more intriguingly, there have long been hints that some bacteria, including *Bifidobacteria* commonly found in yogurt, can improve mood. A common soil microbe, *Mycobacterium vaccae*, has recently been found to cheer up lab mice in experiments by Christopher Lowry, an integrative physiology professor at the University of Colorado at Boulder. Lowry and colleagues showed that infection with *M. vaccae* "alters stress-related emotional behavior" in mice by activating neurons producing serotonin, the neurotransmitter affected by Prozac.

Since the days of Pasteur and Koch, to be classified as disease-causing, a bacterium has had to be grown in culture, isolated from all other organisms. As it turns out, however, very few bacteria can be grown in the relatively austere conditions of laboratories. In fact, only about 0.1 percent of all bacteria are currently culturable. Many bacteria don't do well in monoculture, preferring to live in mixed communities of microorganisms. Those living in extreme temperatures and pressures require very specialized equipment to grow in a typical lab.

Developments in gene sequencing have cast light into the murk of the bacterial world. Instead of the old-school method of isolating and growing each type of bacteria separately, microbiologists are just dipping into biological stews to see what genes they contain. Through metagenomics — the high-throughput technology used to sequence the human genome — they analyze multiple samples of genetic material simultaneously, at high speed and low cost.

Beyond the universe of bacterial genes recently discovered in the human gut, surveys of marine microbes are producing similarly staggering numbers of genes and species. This spring, J. Craig Venter and co-authors reported that samples of seawater taken near Bermuda yielded 150 new types of bacteria and more than a million previously unknown genes — this in an area of open ocean thought to be low in nutrients and sparsely populated by microorganisms.

R. John Parkes, a researcher at the University of Cardiff, Wales, studies microbes found in core samples collected by the Ocean Drilling Program from rocks deep below the ocean floor. "For a long time, these deep sediments were thought to be devoid of any life at all," he says. There's life down there, all right, but talk about slow metabolism: When Parke analyzed 4.7 million-year-old organic sediment in the Mediterranean, he estimated the average time it took for resident microbes to reproduce by cell division at *120,000 years*. And he reported finding living bacteria just over a mile *below* the seafloor, in sediments 111 million years old and at temperatures of 140 to 212 degrees Fahrenheit.

Most of the ocean floor — about 70 percent of the Earth's surface — is covered with such sediments, formed by the constant rain of sand and other particles through the water column. Below the sediments are layers of igneous rocks that ooze from long cracks on the seafloor. It's counterintuitive, to put it mildly, to imagine anything would live in this formerly molten rock where it meets the staggering pressure and cold of the lightless deep. But guess what? There may be more life in these rocks at the gates of hell than there is in the relatively paradisiacal environments above.

Oregon State University microbiology professor Stephen Giovannoni and his graduate student Olivia Mason used metagenomics to survey microbes in basalt along the East Pacific Rise southwest of Mexico, in the Juan de Fuca strait off the coast of Washington state and elsewhere. They found that the communities in the rocks were clearly distinct from the sorts of bacteria common in seawater and, as Mason wrote in her 2008 doctoral dissertation, their total biomass may outstrip that of life in the oceans.

These and other new findings suggest that microbes deep in submarine rock may play a heretofore unrecognized role in the regulation of not just the oceans, but the global environment.

Wherever they live, bacteria can take most of the credit for bringing planetary geology into the service of life. They started working on these processes promptly upon their first emergence, perhaps as early as a mere billion years into Earth's 4.5-billion-year history. Both the energy-releasing chemical reactions and the assembly of complex organic molecules necessary for life are, Rutgers University professor Paul G. Falkowski and his co-authors wrote in *Science*, "an emergent property of microbial life on a planetary scale." In fact, they wrote, the genes that enable these processes today "may have been distributed across a common global gene pool, before cellular differentiation and vertical genetic transmission evolved as we know it today."

In other words, bacteria are supreme code monkeys that probably perfected the packages of genes and the regulation necessary to produce just about every form of life, trading genetic information among themselves long before there was anything resembling a eukaryotic cell, let alone the masters of the universe that humans believe humans to be.

Bacteria, says Giovannoni admiringly, are marvels of engineering. "When it comes to biochemistry, they are much better than eukaryotes," he says. "They don't waste things. They're very efficient, very clever. They keep it simple but very elegant and sophisticated."

But just how smart are they, really?

Giovannoni stops short of claiming that bacteria are actually thinking. But the litany of bacterial talents does nibble at conventional assumptions about thinking: Bacteria can distinguish "self" from "other," and between their relatives and strangers; they can sense how big a space they're in; they can move as a unit; they can produce a wide variety of signaling compounds, including at least one human neurotransmitter; they can also engage in numerous mutually beneficial relationships with their host's cells. Even more impressive, some bacteria, such as *Myxococcus xanthus*, practice predation in packs, swarming as a group over prey microbes such as *E. coli* and dissolving their cell walls.

At least one scientist was willing to allow for the possibility of bacterial thinking quite early in the development of microbiology: Alfred Binet, who invented the first reliable intelligence test and who published a book in 1888 called *The Psychic Life of Microorganisms*. And today the idea of thinking microbes is gaining ground. Marc van Duijn and colleagues at the University of Groningen in The Netherlands point out in the June 2006 issue of *Adaptive Behavior* that the presence of "the basic processes of cognition, such as perception, memory and action" in bacteria can now be "plausibly defended." And bacteria that have antibiotic-resistance genes advertise the fact, attracting other bacteria shopping for those genes; the latter then emit pheromones to signal their willingness to close the deal. These phenomena, Herbert Levine's group argues, reveal a capacity for language long considered unique to humans.

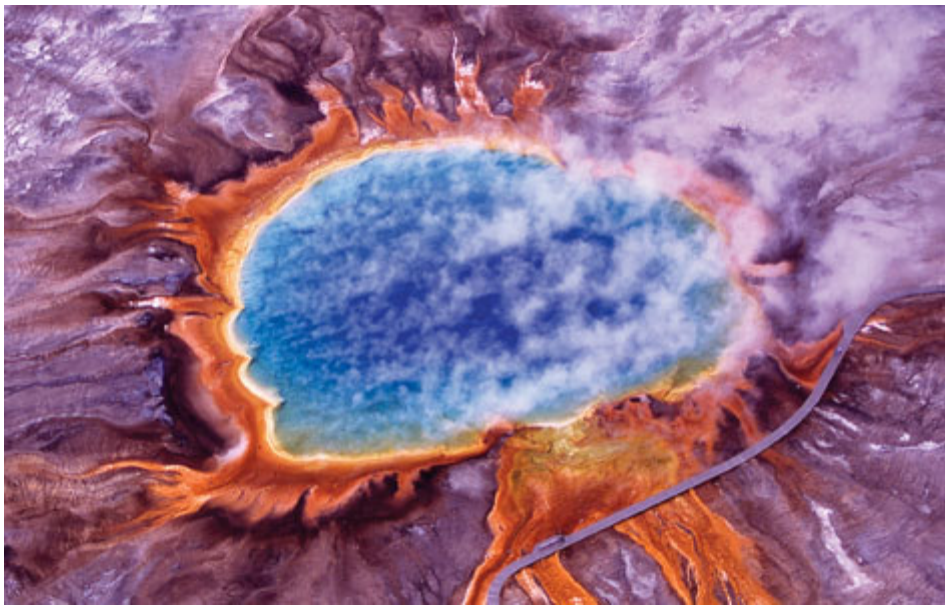
One way to get around the conclusion that bacteria think the way humans think is to say that all the complexity in the world emerges from the simple actions of many "dumb" actors — biological molecules and individual cells, whether they are elegantly differentiated parts of a multicellular organism or bacteria and archaea. In this view, neither some overriding sentience nor individual organisms have any influence over the process.

So maybe bacteria are just computers, which so far, despite humans' unending fantasies of conscious machines, aren't yet really thinking. But University of Chicago microbial geneticist James Shapiro believes they come extremely close. He sees bacteria as consummate practitioners of information management, plus a bit more. They "have ways of acquiring information both from the outside and the inside," he says, "and they can do appropriate things on the basis of that information. So they must have some way to compute the proper outcome." It is these "sophisticated information processing capacities," Shapiro wrote in the paper "Bacteria Are Small but not Stupid," that represent "another step away from the anthropocentric view of the universe. … Our status as the only sentient beings on the planet is dissolving as we learn more about how smart even the smallest living cells can be."

On the other hand, Tufts University philosopher of science Daniel Dennett, a prominent member of the emergent complexity camp, will only grant bacteria "semi-smart" status. Unlike bacteria, human neurons combine in ways that enable intention, Dennett wrote in his 1996 book *Kinds of Minds*. This intentionality is what he thinks sets us apart from the single-celled among us. We possess "different software — the information that organizes the teamwork of all those semi-smart robots," he says.

But this raises the question: Is some nonhuman software organizing the teamwork of all those nonhuman semi-smart robots, aka bacteria? For this would be the truly radical argument: that bacteria — demonstrably integrated deeply and broadly into the entire planet, shaping its geochemistry, creating substrates and chemical processes that support the development of complex organic molecules, regulating the cycling of energy and nutrients both in "higher" organisms and their environments — constitute a kind of distributed awareness encompassing the whole planet. That not only are bacteria in a given local environment busy texting each other like mad, but the entire planet may consist of a giant Microbial World Wide

Web.



An aerial view of Grand Prismatic Spring in Yellowstone National Park. This hot spring is about 250 by 300 feet. The photo shows steam rising from blue water, surrounded by huge mats of brilliant orange algae and bacteria. (wikimedia)

That bacteria-centric argument is, of course, a hazy, metaphysical Gaian fantasy worthy of *Avatar*. In a more down-to-earth assessment, it is clear that bacteria are not what the general run of humans thought they were, and neither are humans. Bacteria are the *sine qua non* for life, and the architects of the complexity humans claim for a throne. The grand story of human exceptionalism — the idea that humans are separate from and superior to everything else in the biosphere — has taken a terminal blow from the new knowledge about bacteria. Whether humanity decides to sanctify them in some way or merely admire them and learn what they're really doing, there's no going back. And if there's any hope of rebalancing the chemistry of a biosphere deranged in two short centuries by humans, it very likely lies in peaceful coexistence with the seemingly brilliant, deceptively simple life-forms comprising the domain Bacteria.