Bacteria as Multicellular Organisms

They differentiate into various cell types and form highly regular colonies that appear to be guided by sophisticated temporal and spatial control systems

by James A. Shapiro

Without bacteria, life on earth could not exist in its present form. Bacteria are key players in many geochemical processes, including the fundamental nitrogen, carbon and sulfur cycles, which are critical to the circulation of life's basic elements. If these processes were to grind to a halt, the planet's soils, waters and atmosphere would become inhospitable for life. Yet in spite of such global importance, the notion has persisted that bacteria are simple unicellular microbes.

That view is now being challenged. Investigators are finding that in many ways an individual bacterium is more analogous to a component cell of a multicellular organism than it is to a free-living, autonomous organism. Bacteria form complex communities, hunt prey in groups and secrete chemical trails for the directed movement of thousands of individuals.

Already at the beginning of this century investigators had evidence that bacteria live communally in the soil. Martinus Beijerinck of the Netherlands discovered that *Rhizobium* bacteria infect the roots of leguminous plants, where they form organized multicellular structures that function as factories for nitrogen production. At about the same time Sergei Winogradsky, working in Paris, elucidated the role bacteria play as decomposers of cellulose in the global carbon cycle. Winogradsky was also one of the first microbiologists to observe bacteria directly in the soil, where he found that few exist as isolated cells; most live in groups adhered to soil particles. Similar group behavior was well known in the laboratory, where bacteria formed distinctive colonies on petri dishes or adhered as organized populations to the walls of culture flasks.

In spite of these early observations, the image of bacteria as unicellular organisms has persisted over the years. In large part this can be attributed to medical bacteriology. Disease-causing organisms are commonly identified by isolating a single cell of the suspected pathogen, growing a culture from that cell and showing that the resulting pure culture gives rise to the disease in question. The possibility that infections of the human body involve multicellular aggregations of bacteria is normally not even considered.

Indeed, many existing theories of bacterial growth, physiology and genetics are formulated exclusively in terms of the isolated bacterium. From an epistemological standpoint this emphasis on the single cell is curious. In practice most research is carried out on cell populations. An enzyme measurement, for example, may be based on an extract from 100 million cells, but conclusions based on the results are often made under the assumption that every bacterium in a population is more or less the same. Such a premise may simplify the interpretation of experimental results, but it is a simplification that is likely to prove invalid in many cases. How exceptional—or how common—are multicellular features in bacteria? In investigating this question I have concluded that most—perhaps virtually all—bacteria lead multicellular lives.

Examples of multicellularity among the bacteria abound; indeed, some of the complex biochemical processes performed by bacteria could not be carried out as effectively without organized groups. Photosynthesis is a process that illustrates this point in several ways. Photosynthetic bacteria, like green plants, rely on solar energy to convert carbon dioxide into organic chemicals. One group of photosynthetic bacteria, known as the cyanobacteria, often grow as connected chains of cells or as intertwined mats; they contain a form of chlorophyll and in many ways resemble multicellular algae. For many years, in fact, the cyanobacteria were thought to be members of the plant kingdom. The multicellular organization aids in light harvesting but yields other benefits too.

Anabaena, an inhabitant of freshwater ponds, is one of the best-known of the photosynthetic bacteria. *Anabaena* is capable of both photosynthesis and nitrogen fixation. These two biochemical processes are incompatible within a single cell because oxygen, produced during photosynthesis, inactivates the nitrogenase required for nitrogen fixation. When nitrogen compounds are abundant, *Anabaena* is strictly photosynthetic and its cells are all alike. When nitrogen levels are low, however, specialized cells called heterocysts are produced. The heterocysts lack chlorophyll but synthesize nitrogenase, an enzyme with which they are able to convert nitrogen gas into a usable form.

James W. Golden and Robert Hasel-

JAMES A. SHAPIRO is professor of microbiology at the University of Chicago. He earned his bachelor's degree in English at Harvard College in 1964 and was awarded a Marshall Scholarship for postgraduate study at the University of Cambridge, where he received his Ph.D. in genetics. He spent a year as a postdoctoral fellow at the Pasteur Institute in Paris, almost two years as visiting professor at the University of Havana and several months at Tel-Aviv University; he was involved in the U.S.-U.S.S.R. microbiology exchange program from 1975 to 1978. In 1973 he joined the faculty at Chicago. This is Shapiro's second article for SCIENTIFIC AMERICAN.

korn of the University of Chicago have shown that differentiation in *Anabaena* involves a form of controlled genetic engineering. In the course of heterocyst differentiation a specific DNA rearrangement occurs that results in the creation of a complete coding sequence for one of the subunits of nitrogenase. Such a rearrangement occurs only in cells that are differentiating to form heterocysts. Comparable DNA rearrangements are involved in the formation of specialized immune-system cells in vertebrates.

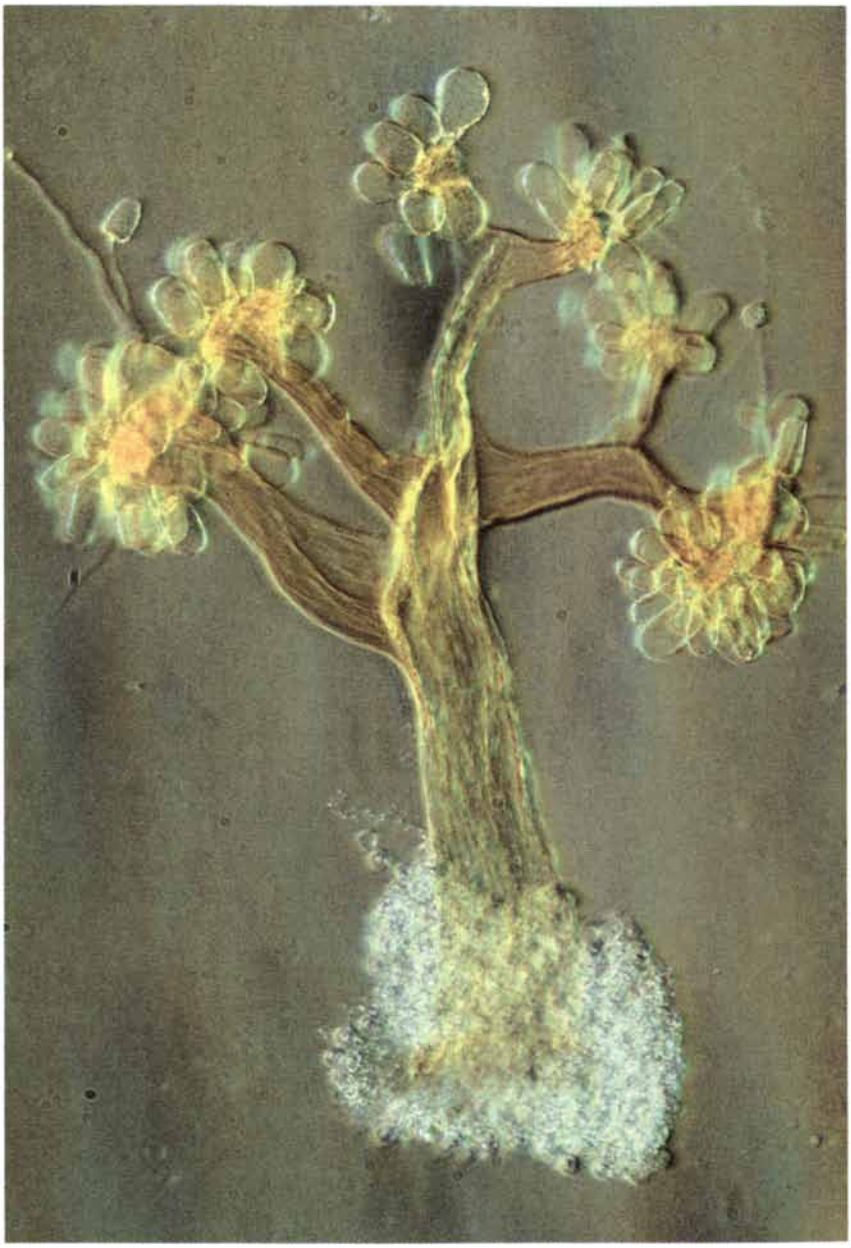
In addition there are submicroscopic channels within each *Anabaena* filament that connect the two kinds of cells. The transport of cellular products (fixed nitrogen to the photosynthetic cells and photosynthetic products to the heterocysts) takes place by way of these channels. In overall character, then, it can be said that *Anabaena* functions more like a multicellular organism than a unicellular one: it relies on division of labor among its cells to carry out specialized and incompatible chemical processes.

More spectacular examples of multicellular behavior can be found among the Myxobacteria, the most morphologically complex of all bacteria. Their elaborate fruiting bodies rival those of fungi and slime molds and have long been an object of scientific curiosity. Myxobacteria are social creatures par excellence and their intriguing, almost psychedelic patterns of aggregation and movement have been recorded in a fascinating series of time-lapse motion pictures produced by Hans Reichenbach of the Society for Biotechnological Research in Braunschweig and his collaborators at the Institute for Scientific Film (I.W.F.) in Göttingen.

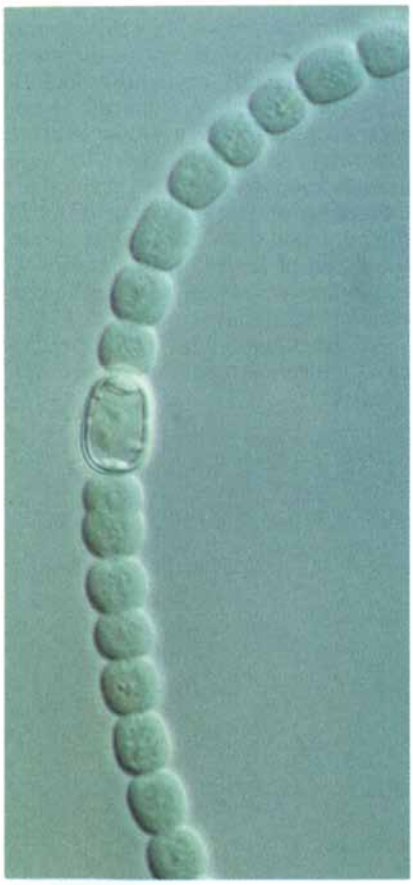
Unlike many bacteria, which periodically enter a dormant stage as individual spores, many Myxobacteria never exist as single cells. Instead they enter dormancy in the form of a multicellular cyst that eventually germinates and spawns a ready-made population of thousands of individuals. Each cyst founds a new population; as the bacteria become more numerous and dense, a number of sophisticated events specific to multicellularity take place. Trails of extracellular slime are secreted and serve as highways for the directed movement of thousands of cells, rhythmic waves pulse through the entire population, streams of bacteria move to and from the center and edges of a spreading colony, and bacteria aggregate at specific places within the colony to construct cysts or, in some species, to form elaborate fruiting bodies. Movement is highly coordinated: when the population migrates over agar, it displaces itself as an intact unit. When an individual cell moves a few microns beyond the edge, it quickly pops back into place as though drawn by an elastic thread.

Even those species of Myxobacteria that do enter dormancy as single-cell spores are social throughout much of their life cycle. When two cells of *Myxococcus virescens* meet, for example, they go through a characteristic ritual: they align themselves side by side and either move off in the same direction or rub alongside each other before separating. Daughter cells can be observed taking part in a similar routine following cell division. These bacteria literally keep in touch with each other!

Predator-prey relationships exist in the microbial world just as they do in the world of larger organisms. Several predatory species of Myxobacteria feed by secreting enzymes that dissolve the outer cell layer of other microorganisms; when the cells burst,



MULTICELLULAR FRUITING BODY of *Chondromyces crocatus,* a species in the group Myxobacteria, is magnified 268 diameters. The structure consists of a central stalk that branches to form specialized clusters of single-cell spores. When the clusters burst, the spores disperse to form new colonies. The micrograph was made by Hans Reichenbach of the Society for Biotechnological Research in Braunschweig.



ANABAENA, **a photosynthetic cyanobacterium, forms filaments of cells in freshwater ponds. Most of the cells are photosynthetic, but when nitrogen levels are low, heterocysts develop. The heterocysts, which are capable of nitrogen fixation but not photosynthesis, are larger than the photosynthetic cells and have special storage granules for nitrogen-rich compounds. The Nomarski micrograph was made by the author; the cells are enlarged 1,625 diameters.**

the myxobacteria absorb their contents. One species, *Myxococcus xanthus,* has evolved a specialized method of prey capture in response to its aquatic environment. In water it cannot release its digestive enzymes because they would immediately be diluted, as would the prey's nutrients. Jeffrey C. Burnham and his colleagues at the Medical College of Ohio have shown that instead *M. xanthus* constructs spherical colonies containing millions of bacteria. The colonies surround suitable prey organisms, trapping them in pockets on the surface of the sphere, where both the digestive enzymes and the prey contents can be effectively corralled.

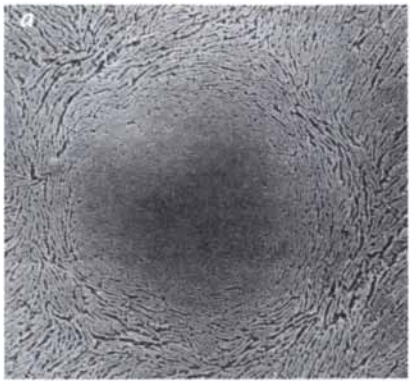
Over the past decade A. Dale Kaiser of the Stanford University Medical School and his colleagues have studied the genetic basis of communication and movement in *M. xanthus.* By searching for mutants that have lost the ability to spread or to form fruiting bodies, they have identified specific regions of the organism's DNA that control for aggregation, motility and differentiation. They found that motility in *M. xanthus* is under the control of two different systems. The *A* (for adventurous) system enables individual cells to move across the substrate; the *S* (for social) system controls the movement of groups of cells. If either system is defective, the cells are still able to spread, but they do so abnormally. If both systems are defective, the cells cannot spread at all. The two systems are surprisingly complex and a great deal of specific genetic information is required for each to be operative. A mutation affecting any one of 23 different genetic loci will eliminate the *A* motility system; at least 10 different loci control the *S* system.

Kaiser and his colleagues have also begun to unravel some of the ways *M. xanthus* cells communicate with one another. They accomplished this by combining different mutant cells that were defective for the same trait but in which the defect resulted from mutations at different loci. They found that when two motility-defective mutants are combined in the same petri dish, they regain motility as long as both mutants stay together. Similarly, if two sporulation-defective mutants are mixed in culture, they will form normal fruiting bodies and sporulate. In some instances such mixed-cell complementation is now known to be mediated by the production of extracellular substances; in other cases it may result either from direct cell-to-cell contact or from the physical presence of two complementary cell types.

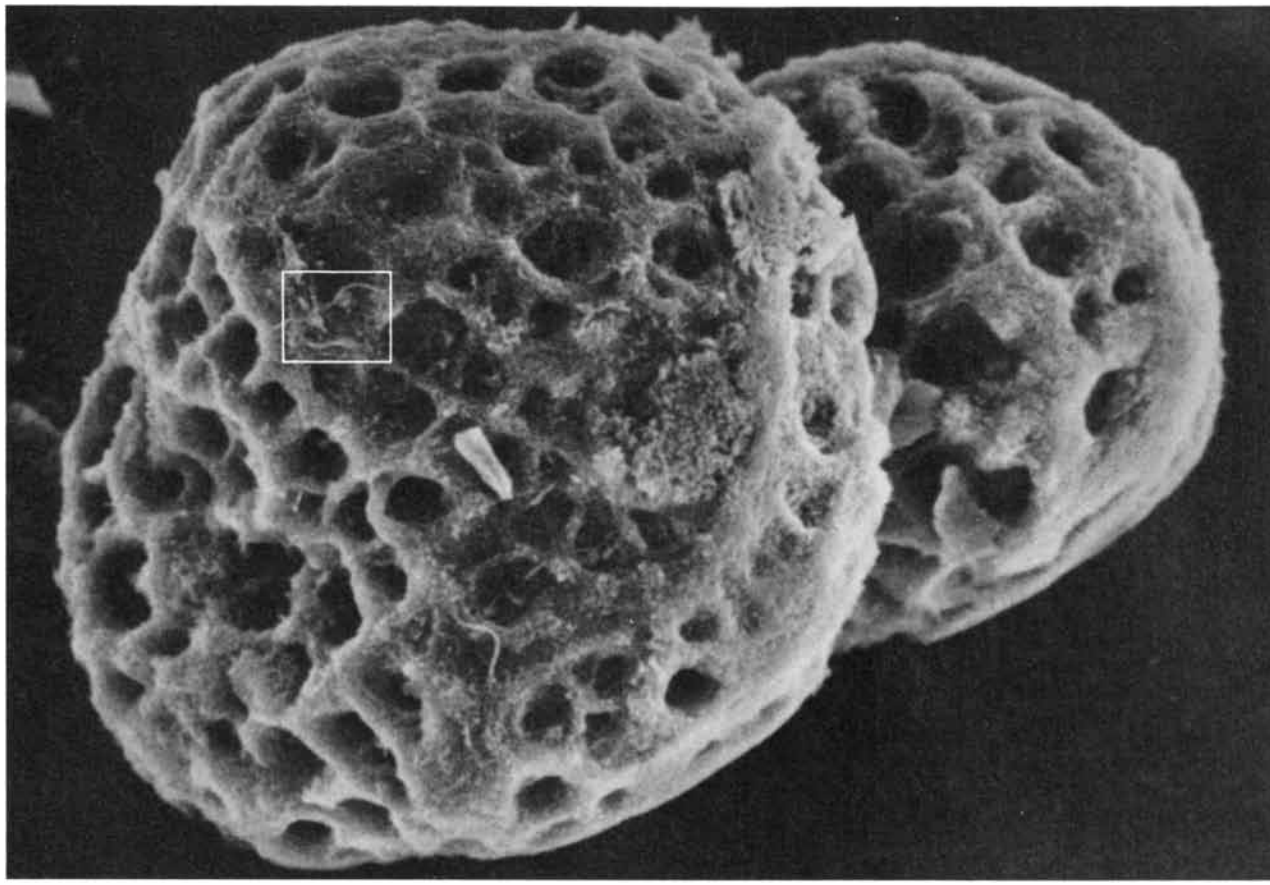
My own studies of multicellular behavior in bacteria began, as is often the case, as the result of a chance observation. A little over five years ago I was experimenting with a genetic-engineering tool, designed by Malcolm J. Casdaban of the University of Chicago and his students, in order to study enzyme expression in *Pseudomonas.* The technique enabled me to join the genes for certain *Pseudomonas putida* enzymes with the DNA sequence from *Escherichia coli* that encodes the enzyme beta-galactosidase. The advantage of beta-galactosidase as a genetic-engineering tool is that it causes certain chemicals to turn color when they are exposed to it. If the beta-galactosidase sequence is linked to the gene for the enzyme under study and the recombinant DNA is inserted into *Pseudomonas,* then when the bacteria are grown on agar containing those chemicals, the amount and distribution of color is a direct measure of the gene's expression.

When I plated my recombinant strains of *P. putida* on such indicator agar, I was astonished to find that every colony exhibited a characteristic flowerlike pattern of staining. I repeated the experiment with engineered *E. coli* and with strains of naturally pigmented bacteria, such as *Pseudomonas cepacia, Serratia marcescens* and *Chromobacterium violaceum.* Each produced its own unique flowerlike pattern. The fact that different strains and species produced distinctive colonies (including species that were naturally colored and not subjected to genetic manipulation) gave me reason to believe colony growth in bacteria is a highly regulated process and is under some form of temporal control. Subsequent studies confirmed that hypothesis. It is now clear to me that colony organization follows certain general rules, which help to explain the existence of general patterns.

The colonies tend to assume a circular configuration, growing outward by adding cells to the perimeter. As a colony spreads across the agar, it is apparent that the pattern of growth consists of both concentric and radial elements. The concentric elements are rings that encircle the colony; the radial elements, or sectors, look like slices of pie. Each sector consists of outwardly growing progeny descended from a common ancestor. Some grow better than others and expand, whereas other sectors merely hold their own or even disappear as the colony gets bigger.



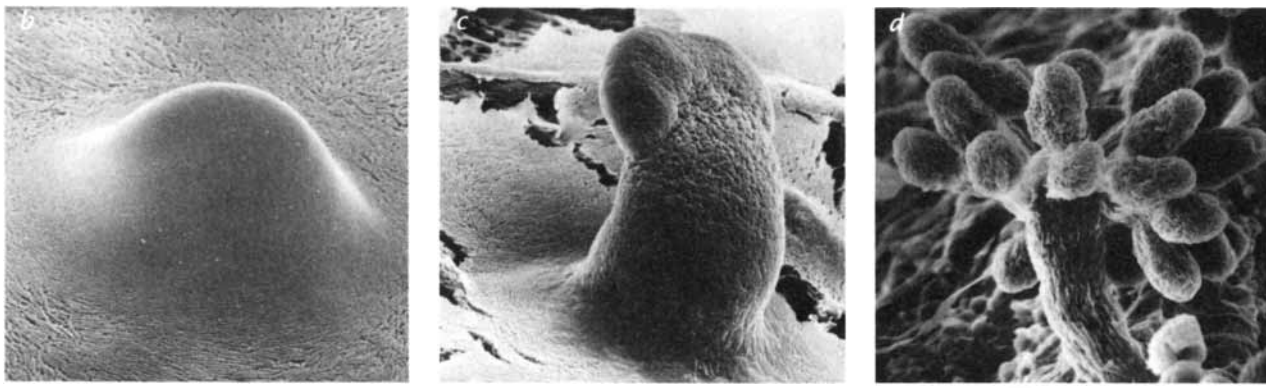
FORMATION OF FRUITING BODY in the Myxobacteria follows a characteristic sequence of steps, as is shown from the far left in these scanning electron micro-



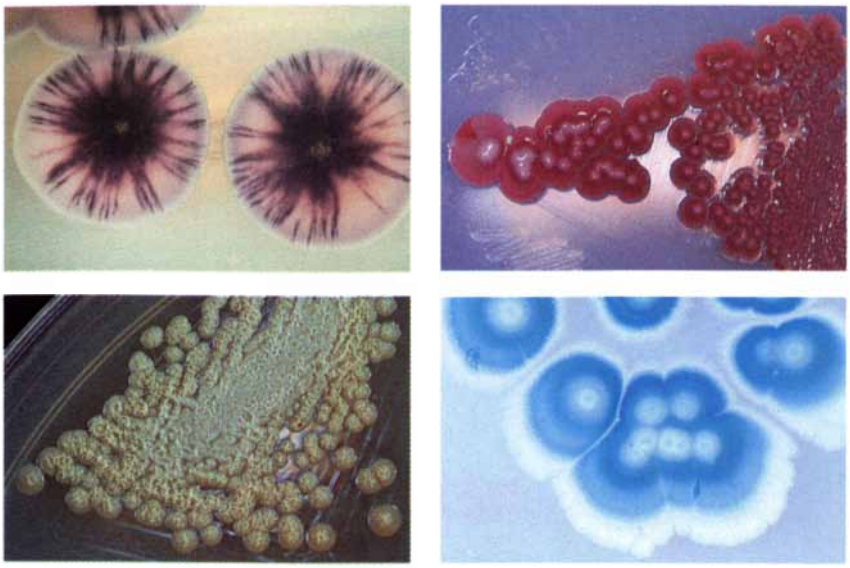
PREDATORY SPHERES are formed by millions of individual cells of *Myxococcus xanthus* as a means of capturing prey in an aquatic environment. Microscopic prey, such as the cyanobacterium *Phormidium luridum* (*inset*), stick to the colony and are eventually digested within pockets on the sphere's surface. The spheres are enlarged 440 diameters in this scanning electron micrograph made by Jeffrey C. Burnham, Susan A. Collart and Barbara W. Highison of the Medical College of Ohio.

In many cases it is possible to select individual cells from different sectors, grow them in culture and show that the cells in one sectorial culture have heritable properties differing from those of the cells in another sectorial culture; often cells from different sectors can be distinguished on the basis of differences in their DNA. Recently N. Patrick Higgins of the University of Alabama Medical School and I found that differences in DNA between distinct sectors and concentric zones can sometimes be visualized directly by picking colonies up on filter paper, extracting their DNA in situ and then applying radioactive probes to detect specific sequences.

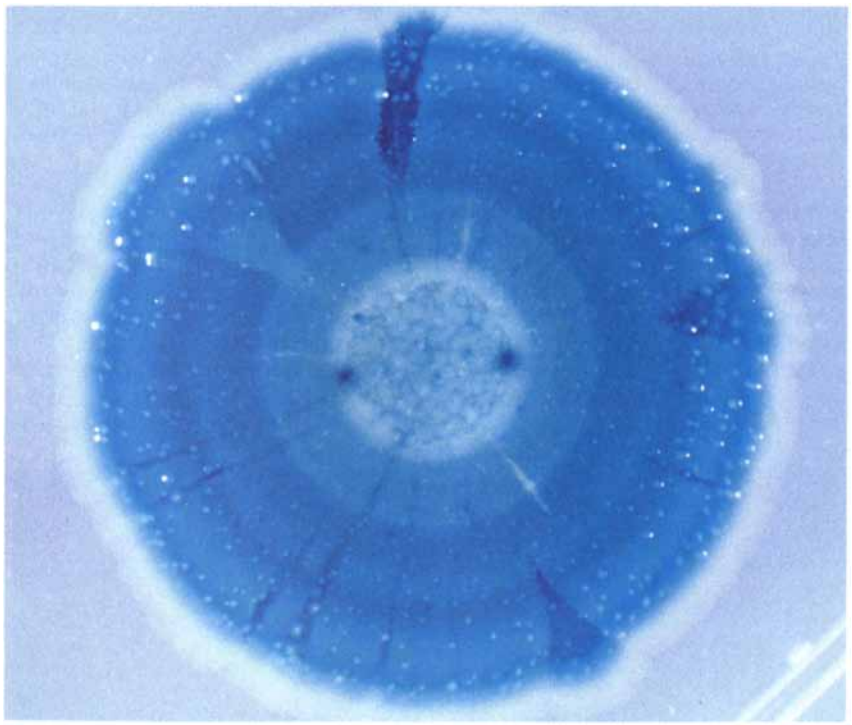
The concentric elements in a colony are less familiar than the sectors and hence more puzzling. The cells in a concentric zone or ring share a common property (such as the level of expression of beta-galactosidase activity) but are not related by common ancestry; they are directly related to bacteria in the preceding and succeed-



graphs tracing the morphogenesis of *Stigmatella aurantiaca*. At first cells form aggregation centers. As the centers accumulate bacteria they bubble upward until the vertical stalk is complete. In some species, such as this unidentified one from the Indiana University campus, the stalk is elaborately branched (*far right*). The *S. aurantiaca* fruiting body is enlarged 450 diameters. Micrographs were made by Gabriela M. Vasquez, Frank Qualls and David White of Indiana University.



FLOWERLIKE COLONIES can be produced by streaking bacterial cultures over an agar plate. Each colony (when it is not crowded) assumes a pattern characteristic of its strain. *Chromobacterium violaceum* (*top left*) naturally produces the pigment violacein and forms purple colonies. *Serratia marcescens* (*top right*) synthesizes prodigiosin; it forms bright red colonies once thought to be drops of blood. *Pseudomonas cepacia* (*bottom left*) is yellow and has a unique surface texture, the result of cell aggregation at the surface. An *Escherichia coli* colony (*bottom right*) carries genetically engineered DNA sequences encoding the enzyme beta-galactosidase; where the enzyme is expressed the colony turns blue. The colonies are at various magnifications.



E. COLI colony was grown from a single drop of culture that contained thousands of cells. The highly regular, intricate pattern of pigmented rings is characteristic of certain genetically engineered *E. coli* colonies stained for beta-galactosidase activity. Pie-shaped sectors, within which the control of enzyme synthesis has changed, are also apparent. The sectors at five o'clock and ten o'clock have curved edges, indicating that the bacteria within these regions spread faster than the rest of the colony. The concentric rings that run through the ten o'clock sector are displaced outward, suggesting that changes in enzyme activity occurred at similar times both inside and outside the sector. This colony was approximately a centimeter in diameter.

ing zones, not to one another. If the organization of the colony into distinct concentric zones cannot be explained by heredity, how might it be explained? Some system must exist that bestows common properties on bacteria within a ring and distinguishes them from bacteria in other rings.

One set of clues to the origins of concentric patterns lies in the different ways the sectorial and concentric elements interact with one another. Photographs of colonies often show that concentric rings persist through sectors that grow faster than the rest of the colony. The resulting pattern contains rings that are stretched outward. The stretching shows that the rings are formed not at specific positions on the agar (that is, at particular distances from the center) but at a specific time in the course of colony development. This suggests bacteria have biological clocks that enable them in some way to program cellular differentiation at specific times during development. The rhythmic pulsations of spreading myxobacterial colonies also reflect the operation of a clocklike mechanism. Both biological clocks and the temporal control of development, previously unknown in bacteria, are important features of higher organisms.

Examination of the surface textures of a colony indicates that cellular differentiation also takes place at the level of cellular aggregation. When light is reflected from a colony, various surface textures that are as organized as the pigmentation patterns and also show radial and concentric elements become visible. In many cases the two patterns coincide: a sector defined by color may also display a novel surface structure, and a ring may stand out on the basis of both its distinctive color and its topography.

Clearly colony organization involves more than the distribution of cells with simple biochemical differences. In order to study structural patterns more precisely, I turned to the scanning electron microscope, which visualizes surfaces at high magnification with great depth of field. The scanning electron micrographs revealed that colonies of *P. putida* and *E. coli* are made up of highly differentiated cells that often form distinctive multicellular arrays coincident with the macroscopic organization of the colony. They also revealed that each colony secretes extracellular materials, some of which form a skin or framework over its surface.

It was clear from these studies that

biochemical activity within a bacterial colony is highly organized and spatially restricted: cells in different regions of the colony have different shapes and biochemical properties. In order to identify the unknown factors that control multicellular growth in bacteria, I began to study swarm colonies. As the name implies, these are colonies that grow quickly and cover a large surface area, two characteristics that make them ideal for laboratory experimentation.

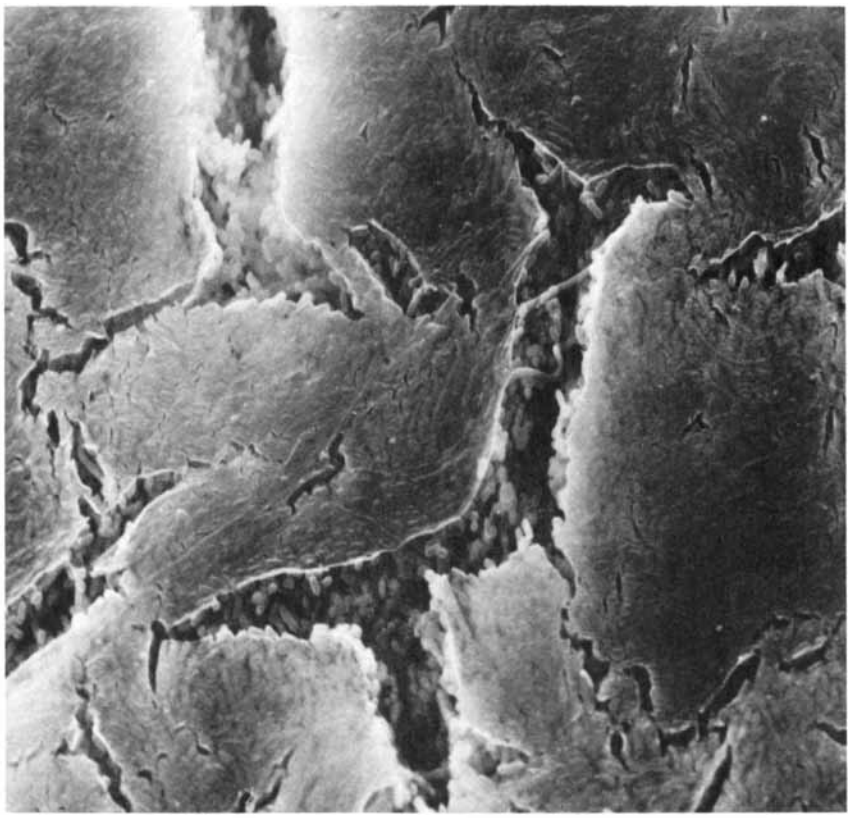
Swarm behavior can be observed in many taxonomically distant species of bacteria. I have focused on one species: *Proteus mirabilis*. Like the Greek god Proteus, this bacterium assumes different forms, producing striking configurations in a petri dish. Over the years two key features of *Proteus* colonies have been noted. One is that there are at least two very different types of cells in a colony: long swarmer cells covered with hundreds of flagellae and short nonswarmer cells with few flagellae. The second feature is that colony development occurs as a tightly programmed rhythmic process.

Swarm colonies develop from an initial population of short nonswarmer cells. As the short cells divide, long swarmer cells begin to appear. They migrate to the periphery of the colony, where they assemble in groups and then pioneer the expansion of the colony by moving out in a series of swirls. The flagellae that cover the surface of swarmer cells rotate and in so doing somehow propel the cells. (It is easy to understand how the spinning flagellae propel a cell through liquid; how such delicate structures are able to propel bacteria over the highly viscous agar surface, however, remains a total mystery.) Observing swarm colonies under a microscope, one sees thousands of flagellae on dozens of swarmer cells moving in synchrony, creating oscillating waves as the cells spread outward from the periphery. Such exquisite coordination prompted Alexander Fleming, the discoverer of penicillin, to wonder in print if *Proteus* could possibly have a nervous system!

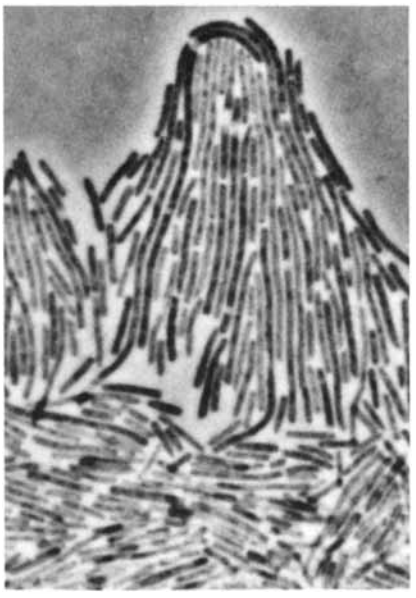
By recording *Proteus* morphogenesis with a time-lapse video camera I have been able to identify distinct periodicities in colony growth, confirming the findings of earlier workers. I discovered that intense activity within a swarm colony can be seen both at the advancing edge, where swarmer cells are rapidly moving outward, and inside the edge, where cell division and streaming activities continue—even when the swarmer cells have stopped advancing. Swarmer cells do not spread indefinitely; they stop after moving a set distance and start spreading again only after a delay, which may be as long as a few hours, depending on conditions such as temperature and the composition of the agar. Swarming is strictly a multicellular activity; an individual cell that gets separated from the rest is unable to advance over the agar unless it is engulfed by another swarmer group, at which time it starts to move again.

Activity inside the edge has its own periodicities and rhythms but is connected to the expansion of the colony as a whole. When the swarmer cells finish one phase of spreading, for example, a series of visible waves composed of more densely aggregated cells moves from inside the swarm zone toward the perimeter. Then there is a thickening of the cell mass in the recently colonized zone and a bubbling of the surface inside the perimeter. These and other exquisitely choreographed postmigration processes produce elaborate textures in the form of terraces on the surface of a fully developed swarm colony.

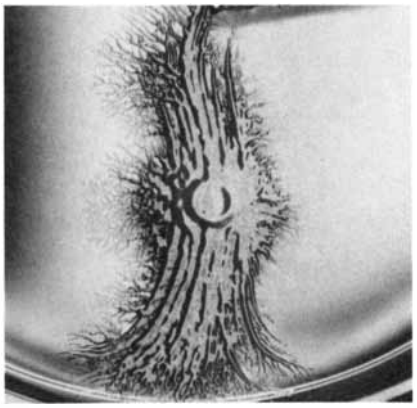
Watching the swarming process, I



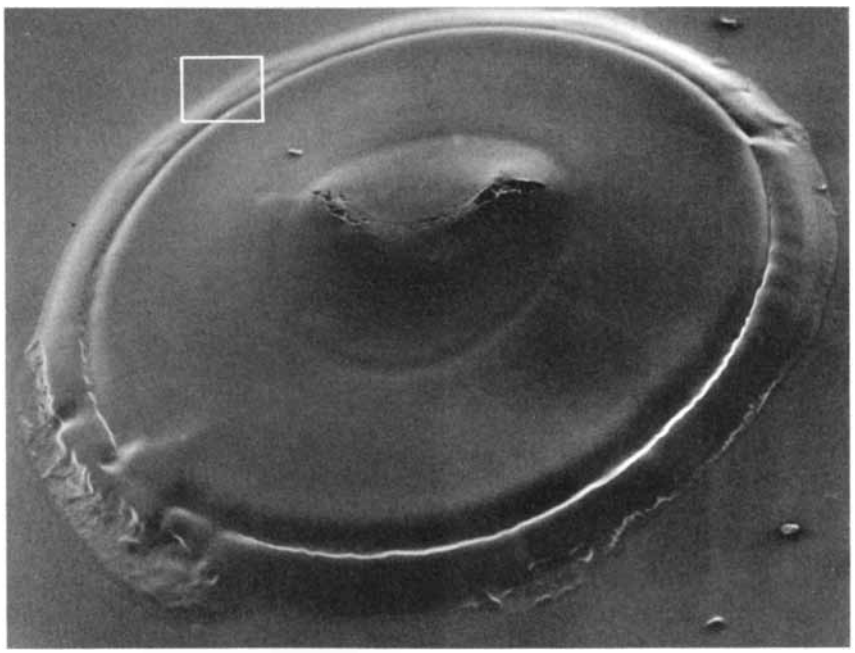
SCANNING ELECTRON MICROGRAPH of a *Pseudomonas putida* colony reveals that extracellular material covers its surface like a skin. This superstructure may in some way facilitate communication among cells of the colony. One long, curved cell can be seen bridging a crack in the skin; such cells may also be involved in intercellular communication within the colony. The colony is enlarged 2,300 diameters.

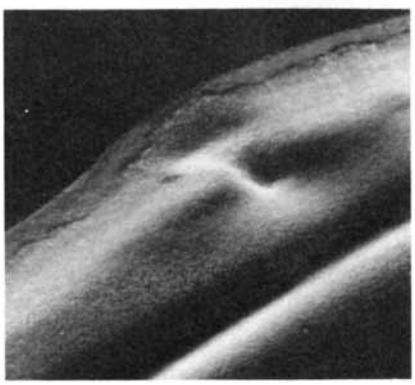


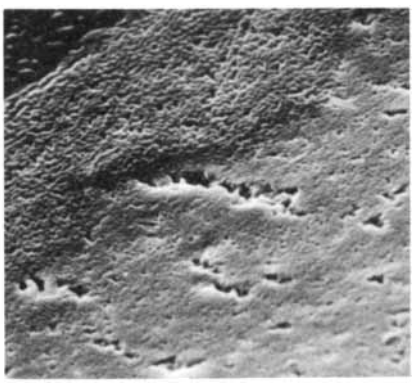
LONG SWARMER CELLS can be seen at the edge of a *Proteus mirabilis* colony. The cells are preparing to move across the agar as a group; they do so by rotating their flagellae in synchrony. The cells are enlarged 600 diameters in this micrograph made by S. A. Sturdza of the Cantacuzino Institute in Bucharest.



PROTEUS MIRABILIS **mutants show geometries that provide clues to the way colony spreading is controlled. The mutant (*left*) forms regular repeating terraces in a nine-centimeter petri dish. If a trench is cut in the agar, however, spreading stops after a few cycles. The fact that swarming is blocked in the shadowed zone indicates that a chemical signal must emanate from the center. Morphogenesis appears to be under whole-colony control; it is not regulated solely by the migrating edge. The mutant (*right*) has lost its circular symmetry and has a markedly different pattern. The bacteria began by forming thick columns along stress lines in the agar; after these columns grew to a certain size they ramified into smaller perpendicular processes that in turn formed smaller branches. This pattern suggests that although the mutant lacked the ability to produce circular colonies, it retained some kind of directional control. The length of this colony was about four centimeters.**





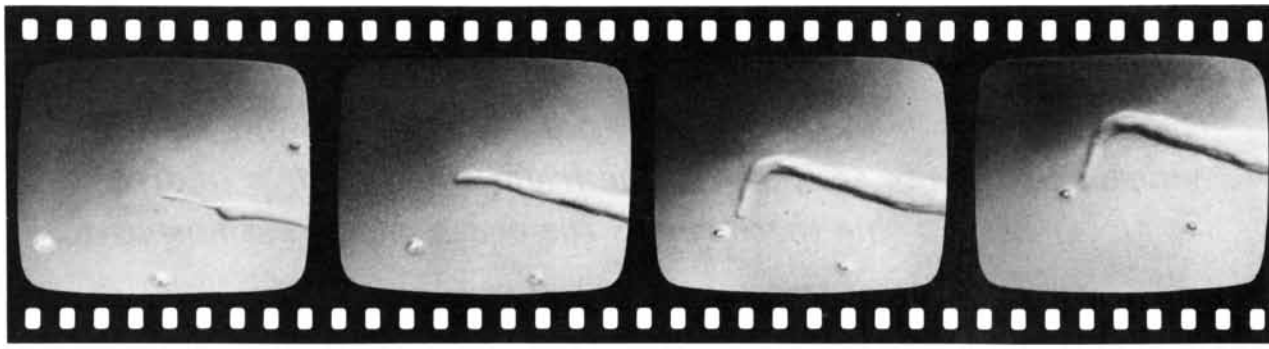


wondered whether it would be possible to learn about the systems that control this intricate and regular behavior. In biological research important clues can come from looking at the response of organisms to unusual circumstances. If conditions in the petri dish changed, would a swarm colony alter its behavior?

Two kinds of evidence suggest that swarming behavior is indeed regulated. One is that when swarming is interrupted by chemical or physical obstacles, or by interference with the growing cell mass, specific morphological responses take place. Observation of the geometries of the swarm colonies after they have been artificially manipulated (or following spontaneous accidents that deform the regular outlines of the colonies) makes it clear that both temporal and directional controls influence colony growth. In particular, chemicals diffusing through the agar appear to play important roles in guiding colony spread.

The second line of evidence is that morphogenesis is under hereditary control. For one thing, each naturally isolated strain of *P. mirabilis* has its own characteristic mode of swarm-colony development. For another, one can obtain from these natural isolates various mutants that can still spread but that have geometries markedly different from those of their progenitors. Some mutants form periodic swarm terraces that are more closely spaced than those of their parents, whereas others have no terraces at all. One particularly striking mutant has lost its circular symmetry altogether and grows in a branching pattern influenced by stress lines in the agar. Clearly the genes that regulate morphogenesis have been altered in these mutants, whereas the ability to swarm has not been eliminated. A detailed biochemical explanation for how morphogenetic control systems might operate in *Proteus* (or in *Myxococcus* or *E. coli,* for that matter) has not yet

DISTINCTIVE MORPHOLOGY of cells in different zones is demonstrated in a series of scanning electron micrographs of an *E. coli* colony. The 68-hour colony (*top*), formed from an initial population of 100,000 cells, was five millimeters in diameter. When the leading edge is enlarged 100 diameters (*bottom left*), a distinct boundary is visible between two groups of differentiated cells. At greater magnification (750 diameters) the outermost zone (*bottom right*) is seen to be made up of large cells arranged irregularly, whereas the inner zone has smaller cells grouped in roughly parallel arrays.



PURPOSEFUL MOVEMENT of *M. xanthus* cells is shown in a series of frames on a video monitor. At the bottom of the screen is a latex bead, five micrometers in diameter, toward which the cells, collectively called a flare, will orient. The tip of the flare turns toward the bead at 18 minutes (*second frame*); at 33 minutes (*fourth frame*) the flare reaches it. After sensing that the bead is inedible the flare will move on. These images were made by Martin Dworkin of the University of Minnesota.

been found. Nevertheless, the hereditary specificity of the developmental phenomena suggest that studying these systems will yield important lessons about coordinating the behaviors of large numbers of bacteria in a spatially and temporally defined way.

The view that bacteria are sentient creatures, able to receive, process and respond meaningfully to external signals, has been gaining ground over the past two decades as investigators spend more time exploring the mysteries of bacterial behavior.

Martin Dworkin of the University of Minnesota has recently provided a graphic demonstration of multicellular responsiveness in the microbial predator *Myxococcus xanthus*. He found that roaming flares, or groups, of *M. xanthus* cells perceive clumps of prey bacteria (or even glass or plastic beads) on an agar surface, make sharp turns toward the objects and then move directly to them. Once there, the *Myxococcus* flares are able to tell whether the objects are edible or not. If the objects are edible, the flares stay to feed; if they are not, the flares turn away and continue their searching behavior. Such purposeful behavior has traditionally been thought to operate only in larger organisms.

What practical value, if any, do these findings have? The biotechnology industry, eager to turn to genetically engineered bacteria as factories for the production of complex biochemicals, will undoubtedly benefit from the knowledge that bacterial cells specialize and control protein synthesis with the aid of intercellular communication signals. In the field of biodegradation the application of bacteria to remove toxic chemicals from polluted soils and water sources may be enhanced by greater understanding of multicellular processes. It may even be possible to introduce multicellularity characteristics that optimize productivity or improve the capacity of specific strains to degrade synthetic compounds. Understanding the behavior of bacteria may also make it easier to monitor the release of genetically engineered organisms.

In medicine greater understanding of bacterial behavior may lead to increased efficacy of drug treatments. J. William F. Costerton and his colleagues at the University of Calgary in Alberta recently described a patient who suffered from recurrent bloodstream infections because a colony of *Staphylococcus aureus* had formed on the lead of his cardiac pacemaker. Individual cells would break away from the parent colony periodically and infect his bloodstream. Although the individual cells were sensitive to penicillin, the colony itself was drug-resistant: like many bacterial colonies, it was protected by a coating of extracellular slime. In order to end the chronic infection the only solution was to remove the pacemaker (and its colony).

In other cases of bacterial pathogenesis there is a clear correlation between the tendency of cells to aggregate and their ability to establish an infection. It has been known for 25 years that the organism that causes gonorrhea, *Neisseria gonorrhoeae*, forms several types of colonies on laboratory media. Cells from one type are virulent, whereas those from another are not. Since a successful infection requires that the disease organism colonize its host, I suspect pathogenesis is directly related to this organism's ability to form multicellular organizations (as reflected in the kinds of colonies it builds).

Bacteriology's early pioneers, such as Louis Pasteur, recognized that there are many lessons to be learned from these smallest of living cells. Today much more is known about the intricacy and complexity of this group of organisms. If, as I have proposed here, bacteria possess elaborate developmental and behavioral capabilities typical of higher organisms, then it is likely that detailed explanations of how these small cells communicate will influence views of information processing in all organisms.

Although bacteria are tiny, they display biochemical, structural and behavioral complexities that outstrip scientific description. In keeping with the current microelectronics revolution, it may make more sense to equate their small size with sophistication rather than with simplicity. There is little reason to doubt that insights gained from studying the interactions of billions of bacteria, living together in a volume of less than a few cubic millimeters, will enhance understanding of all forms of life.

FURTHER READING

NATURE OF THE SWARMING PHENOMENON IN *PROTEUS*. Fred D. Williams and Robert H. Schwartzhoff in *Annual Review of Microbiology*, Vol. 32, pages 101–122; 1978.

MYXOBACTERIA: DEVELOPMENT AND CELL INTERACTIONS. Edited by Eugene Rosenberg. Springer-Verlag, New York, 1984.

ORGANIZATION OF DEVELOPING *ESCHERICHIA COLI* COLONIES VIEWED BY SCANNING ELECTRON MICROSCOPY. James A. Shapiro in *Journal of Bacteriology*, Vol. 169, No. 1, pages 142–156; January, 1987.

The following films are available in the U.S. from Audio-Visual Services, Pennsylvania State University:

BACILLUS CIRCULANS—AUFBAU UND VERHALTEN (*B. CIRCULANS*—GROWTH AND BEHAVIOR). Silent film, E183. Institut für den Wissenschaftlichen Film.

PROTEUS—BEWEGUNGSVERHALTEN (*PROTEUS* SWARMING BEHAVIOR). Silent film, E271. Institut für den Wissenschaftlichen Film.