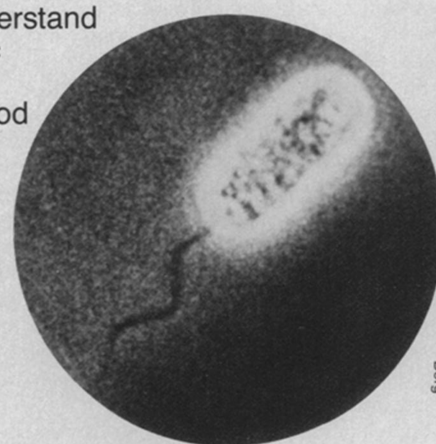
Swimming for the Good Life

Biophysicists and biochemists are beginning to understand how chemotactic bacteria sense and go for the good things of life



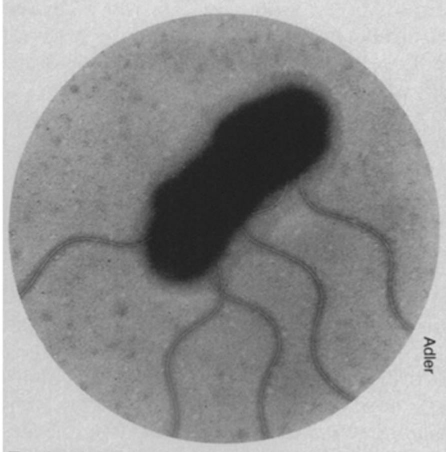
Berg

Bacterium Chromatium okenii *swimming with its flagella wrapped together.*

By DIETRICK E. THOMSEN

Chemotactic bacteria can sense the presence of certain chemical substances in their environment. They tend to swim towards the ones they like and away from the ones they don't like. Some of the attractants are things they eat, but others are things they just seem to like to be near. In the case of the uneaten attractants, scientists speculate that in some distant past there were bacterial ancestors that ate those things. Even though later generations evolved away from eating them, a tendency to like the substances was still inherited. Many species exhibit chemotaxis, but the most commonly studied is the one Julius Adler of the University of Wisconsin calls the "molecular biologists' hydrogen atom," *Escherichia coli.*

Biophysicists and biochemists ask the question, in the words of Edward M. Purcell of Harvard University, "How much physics [or chemistry] does a bacterium need to know?" That is, how does it use the physics and chemistry of its environment and itself to sense the presence of attractants or repellents and move toward or away from them? The consensus of a symposium on the subject held at the recent meeting of the American Physical Society in Detroit is that observers can make some head and tail of the problem, but the middle eludes them. They know something about how the bacterium senses the presence of the chemicals and how it knows when it is swimming toward a greater or lesser concentration of them. They also think they know how the bacterium runs the little motors that move the flagella by which it propels itself. They do not know how the message gets from head to tail, from the parts that sense the chemicals to the parts that drive the flagella.



Adler

Escherichia coli *with its flagella unwound.*

Physically, the world of bacteria is an Aristotelian one (SN: 4/8/78, p. 214). Aristotle's physics is based on the common sense notion that something moves only if it is being pulled or pushed. Isaac Newton, starting the series of developments that gradually divorced physics from common sense, said that that isn't true. A moving body has what you call inertia, and it will just keep on moving until something intervenes to stop it.

In the world of bacteria, Purcell says, inertia doesn't count. It's a very special and interesting case of fluid physics at low Reynolds number. The Reynolds number is the ratio of inertial to viscous forces felt by the moving object. For bacteria the Reynolds number lies between 0.00001 and 0.0001. For *E. coli* particularly it is 0.00003. This means that if a bacterium stops propelling itself, it fetches up dead in the water. For a fish, by contrast, the Reynolds number is 100; a single flick of the fins can send the average fish quite some distance.

The low Reynolds number means that the bacterium can't make progress throwing water back, Purcell says. It can't get anywhere by rowing. It moves by wrapping together the six or eight flagella (long hairs that come out of its body) and making them into a proper, low Reynolds number propeller. One of the big recent discoveries, these observers say, is that the flagella don't flail around aimlessly, but rotate to a purpose.

Unlike the limbs of higher animals, the flagella have no blood or nerve supply, and so can have universal joints and twist full circle. If the flagella are twisting counterclockwise, they wind together into a bunch that forms a low pitch helix, a very good propeller under the circumstances. The organism moves forward in nearly a straight line.

For efficient propulsion, Purcell points out, there must be an optimum balance between head and tail. If Newton's first law does not apply in this environment, his third law certainly does. For every action there is an equal and opposite reaction: The head will spin in the opposite direction to the tail. It turns out that a mass balance that lets the head spin at 7 revolutions per second while the tail goes 140 rps is best. Propulsion then involves expenditure of about a hundred-millionth of an erg per second per bacterium, or putting it another way, half a watt per kilogram of cells. An organism can get this by metabolizing about 3,000 glucose molecules a second. It can get that much feed at a fairly low concentration, Purcell says. The motor is so cheap to run that the organism could swim perpetually.

But it doesn't go forward all the time. From time to time it reverses engines and starts the flagella rotating clockwise. Then the bundle of flagella comes apart, and the bacterium starts to tumble. After a bit of tumbling, the engines reverse again, and the organism runs off in the direction its head happens to be pointing. So it goes, alternating tumbling and running. The directions of the runs do not seem to be deliberately chosen, as a higher organism would move, but random, depending on how the tumbles end. How this action becomes less random in the presence of attractants and repellents is what the research is about.

The motion does seem to become preferential. At the meeting, Adler illustrated experiments in which attractants or repellents were introduced to a petri dish full of *E. coli.* In a fairly short time the bacteria had congregated either where the stuff was or where it wasn't. Further experiments involved a uniform concentration of attractant that was changed over time. In the absence of attractant the bacteria alternated running and tumbling. After introduction of the attractant they did nothing but run for up to five minutes. Gradually, however, they became accustomed to the change and resumed their previous rhythm. If the attractant was removed, the *E. coli* went into a period of wild tumbling until they adjusted again. In experiments where the concentration of attractant or repellent varied over space, the bacteria would lengthen their runs if they were going in the preferred direction. If a tumble happened to turn them in a wrong direction, they would shorten that run.

They sense the presence of the chemicals through spots on their surfaces. The whole surface does not need to be sensitive to one substance. Purcell compares the situation to the electrical capacitance of a sphere. The capacitance of the sphere is the same whether it is an unbroken surface or a wire mesh. Similarly the detection efficiency of the *E. coli* is just as good with tiny sensors scattered over the surface like the nodes of a mesh. This way one and the same organism can be, and is, sensitive to several chemicals.

As the molecules of an attractant diffuse through the water, they occasionally land on one of the appropriate sensors and initiate a chemical reaction. Adler describes the sensors as methylaccepting chemotactic proteins (MCPs). There are four different MCPs, each responding to different kinds of chemicals. "We now know the complete amino acid sequence of all these proteins," he says.

Each of the MCPs is divided into three parts. One part is outside the cell, one embedded in the cytoplasmic membrane of the cell and one inside the cytoplasm. The outside parts, which recognize the attractant, are different for each MCP. The inside parts, which are methyl groups, are similar to one another. "The inside parts must be the beginning of the message," Adler says. Because of the capacity to adapt and disadapt, they must be able to produce an "excitation stuff" at one time and then an "adaptation stuff." The details of the chemical mechanism are not clear. Adler says it may be that MCPs are ion gates to admit some substance X, or they may be enzymes for producing X or for destroying X.

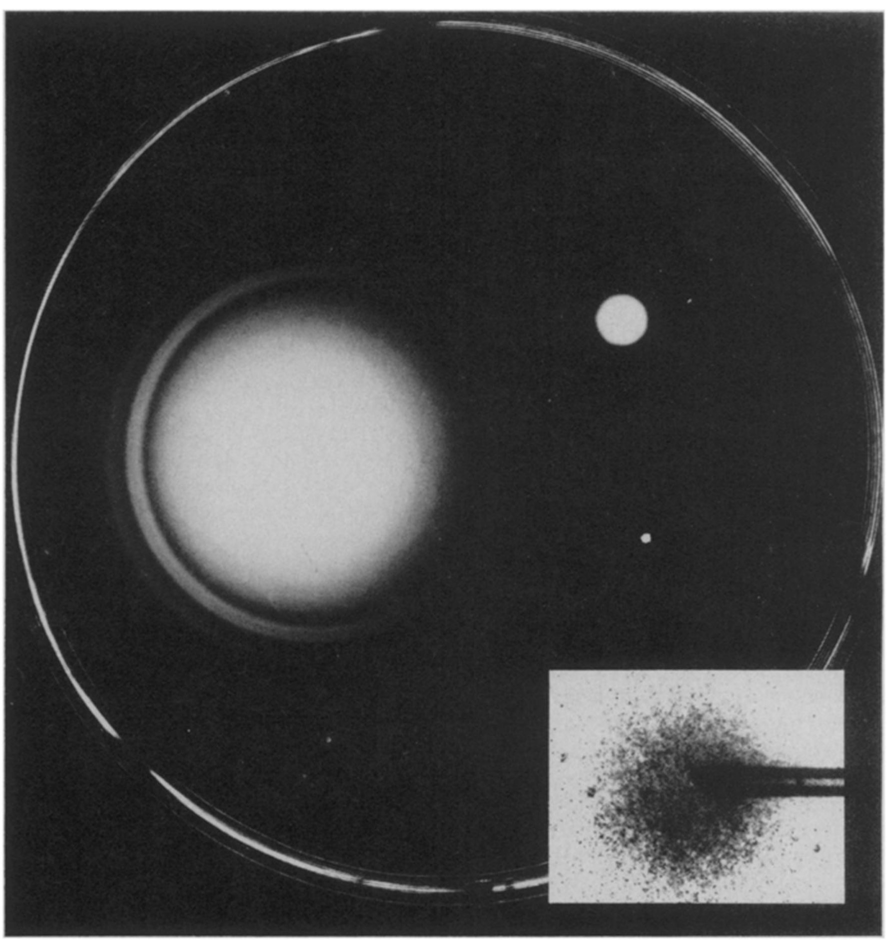
The statistics of the message are another question. Purcell asks how many sensors need to be occupied at once. His further question is how the organism knows it is going in the right direction. Given the physics of the diffusion of molecules in water, *E. coli* is too small to take samples at opposite ends of its body and so determine where the higher concentration is. It has to do it temporally, comparing its situation now with that a fraction of a second ago and being able to tell when it is better or worse off. That means an organism as primitive as a bacterium has to have something like a memory. Purcell asks, "How does a bacterium remember?" Right now it is not a rhetorical question.

Yet somehow the message gets to the bacterium's tail. Howard C. Berg of California Institute of Technology in Pasadena studies the motions of bacteria with a special microscope he designed. With an ordinary microscope, he says, it's impossible to follow a swimming bacterium. It quickly moves out of focus. He designed a microscope that follows a bacterium. It has a feedback system that concentrates on keeping a particular organism in focus at all times and moves the chamber around appropriately. "It's like following a worm through a bucket of sand by moving the bucket," he says.

Berg also grows giant *E. coli,* exceptionally long ones. *E. coli* cannot make septa, he says. They do not divide as other microorganisms do. If you feed them they just get longer. Berg pins down flagella of the big bacteria by attaching them to the dead bodies of smaller ones and tethers them to a glass slide. Then he is ready to watch how they twist and turn when attractants or repellents are added to the water.

From this Berg has deduced something of the motor mechanism. The flagellum is a long thin hair — Purcell says it is about 150 angstroms (an angstrom is one ten-billionth of a meter) in diameter. One end is free, the other is attached by a universal joint to a short rod that sticks through the wall of the cell. "The rod is a drive shaft," Berg says. It terminates in a ring embedded in the cytoplasmic membrane of the cell. This ring turns against another, stationary ring lying outside it in the outer wall of the cell. (The rod passes through this outer ring.) What makes the inner ring turn is electric forces supplied by protons moving through the wall of the cell in response to some electrolytic difference between inside and outside. The motion is not triggered by ATP (adenosine triphosphate) as is the motion of muscles or sperm cells, Berg says.

Thus something is known about how the chemotactic bacterium senses the relevant chemicals and how it drives itself toward them. What is still almost unknown is the middle part. How does the organism compute? How does it take the message from its sensors and tell its motors what to do? □



Adler

Three kinds of E. coli *in same dish with attractant. Large circle, left, is chemotactic variety spreading rapidly as it eats attractant. Upper right circle is non-chemotactic mutant spreading slowly. Smallest circle is mutant unable to swim. Inset shows* E. coli *rushing toward end of pipette that introduces attractant.*