Making sense from bacterial signals

With optimism and a little luck, bacteria may turn out to be simple models for the function of sensory cells. This was the conclusion of participants in an American Chemical Society symposium on Frontiers in the Chemical Senses held in Philadelphia last week.

Displaying that optimism, molecular biologist F. R. Dahlquist of the University of Oregon presented evidence that bacterial "information receivers" may function on the molecular level much like sensory cells in higher organisms. His work is part of a broader study of bacterial "chemotaxis," the ability of the tiny, one-celled organisms to receive, decode, store and act on chemical messages from the surrounding environment.

The study of bacterial chemotaxis has matured remarkably in the past few years. Scientists observed in the late 1800's that motile bacteria (those that move themselves from place to place) will migrate toward certain favorable chemicals and away from unfavorable ones. Only recently have researchers begun to understand how bacteria sense these chemicals and how this sensation leads to a behavioral response, in this case, movement.

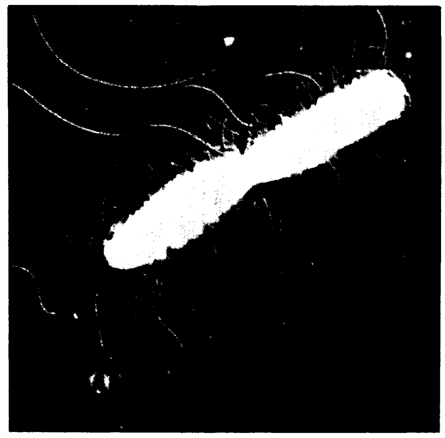
Researchers Julius Adler of the University of Wisconsin, Howard C. Berg of the University of Colorado, D. E. Koshland of the University of California at Berkeley and others have painted a pointillistic picture of what happens when a microscopic organism meets a submicroscopic molecule. Motile bacteria such as *Escherichia coli* and *Salmonella typhimurium* appear almost comical to the observer. The cells swim along in straight runs by rotating their flagella, then stop abruptly and tumble in place. When they recover from the tumble, they follow their "noses" off into a new, randomly chosen direction. As comical as this swimming-tumbling-swimming behavior may seem, however, it is the manifest functioning of a primitive sensory system, motor system and tiny brain all in one cell.

Bacteria, the researchers have shown, have receptors in their outer membranes that bind the chemicals in the liquid world around them. If an attractant is introduced and diffuses toward the cells, forming a concentration gradient in the liquid, the bacterial receptors pick up the early "scent." Somehow, the receptors tell the cell to stop tumbling and start moving up the gradient toward the source of the pleasant chemical. If a repellant is introduced, the receptors sense that, too, and turn off the "tumble generator" so the cell can make a beeline away from the offensive agent. When there is no gradient present (only a constant concentration, instead) the tumble generator is turned on and the cell tumbles and zig-zags in random directions, sampling and resampling the surrounding environment.

When the receptors bind an attractant or repellant, some kind of signal is sent to the tumble generator, or as Berg calls it, the "gear shift." The signal tells the flagella which direction to rotate, causing either straight swimming or tumbling. The nature of that signal and how it is processed and translated into behavior is a highly sought secret. It is, in fact, the central problem in the study of chemotaxis, Dahlquist says, since an answer would likely help explain the way sensory cells in higher animals collect information and translate it into a motor response.

Dahlquist's latest work deals with this question, in part. He presented evidence to the ACS symposium that bacterial binding sites cooperate to help the cell sense gradients. Bacteria are able to respond to a much larger range of concentration than would be predicted by the simple filling of receptor sites. There may be an aggregate of binding sites, Dahlquist says, associated with each receptor. When one site is bound, binding a second site would be more difficult and require a higher concentration of the chemical. When enough binding sites are filled, a signal could be generated and sent to the data processing center to turn the tumble generator on or off.

The filling of these binding sites could perhaps lead to a membrane de-



S. typhimurium (× 7,600) showing flagella, effectors of motor response.

polarization, Dahlquist says. This is where the optimism comes in. "No one knows for sure if there is a membrane depolarization, and you can't place an electrode in or near a bacterial cell to measure electrophysiological response because the cells are just too small." But, despite their small size, if there is a depolarization or an electrochemical equivalent, bacteria could be a good system for learning about sensory cells. *E. coli* and *S. typhimurium* are well characterized genetically and biochemically, Dahlquist says. By finding mutants with improperly functioning sensory traits, one could, by comparison, determine the genes and proteins involved during proper functioning.

Current and future studies will center on isolating receptor proteins, hopefully in working order, and looking for the key to information processing, Dahlquist says. □

Why medicine needs basic science

One of the world's largest scientific meetings—the annual meeting of the Federation of American Societies for Experimental Biology—rolled around again this week in Atlantic City. This year's meeting offered a new kind of symposium entitled, "The significant contribution of biomedical research to the control of disease." In essence, the meeting reflected biomedical scientists' growing awareness that the public is skeptical of biomedical research that does not have obvious, immediate clinical applications, and that if they hope to receive continuing funds for this kind of research, they must defend its ultimate practical importance.

Few major advances in clinical medicine have come about without a basic understanding of the diseases they combat, Lewis Thomas, president of the prestigious Memorial Sloan-Kettering Cancer Center in New York City and author of the award-winning book of essays *Lives of a Cell* (SN: 8/3/74, p. 77), told the group. Even with the smallpox vaccine of the 18th century, Thomas said, "Jenner . . . had a remarkably prescient hunch about what he was up to." As for the conquest of infectious diseases by antibiotics in the 1930's and the 1940's, Thomas said, it would not have been possible without basic microbiology, immunology and virology research harking back to the 19th century.

Basic research has also been indispensable to advances in cancer treatment, Emil Frei III of Harvard Medical School said. For instance, biomedical scientists have used their basic understanding of how certain antibiotics interact with DNA to rationally design antibiotics that counter tumors. And test-tube studies indicate that cancer cells are rapidly growing cells, and that cells that turn over frequently are more susceptible to drug action. These findings provide a rational basis for cancer chemotherapy. "Some years ago we showed that BCG [tuberculosis vaccine] was able to cause regression of tumors in mice," Baruj Benacerraf, also of Harvard Medical School, reminded the symposium audience. "Only now is it being considered for clinical therapy."

Clinical advances in heart disease also stem from biomedical research, particularly of the non-mission-oriented kind, Eugene Braunwald of Peter Bent Brigham Hospital in Boston said. One of the most dramatic advances in medicine during the past 25 years has been the development of open-heart surgery, and only the last phase was mission-oriented research: the development of the pump-oxygenator (artificial heart and lung) apparatus. However, even the original goal of the surgeon who invented this apparatus was not open-heart surgery. It was designed to keep a patient with a blood clot blocking the main artery to the lung alive long enough to remove the clot surgically.

Thus scientists, for the most part, want funds for basic biomedical research with as few goal-oriented restrictions as possible. But with increasing costs of biomedical research, the public prefers to fund research with immediate clinical spin-off. The National Cancer Act of 1971 is a prime example. "The fact that there are two sides is something that most of us in this room have been reluctant to face," Thomas admitted. "We have had so strong a preference for our side that we tend to ignore the major issues of the disagreement, on the assumption that they will go away if we are patient. They will not go away. It is a genuine argument, with two genuine intelligible points of view, and the way it comes out may well determine the course of both biomedical science and the practice of medicine for the rest of the century and beyond." □

Twin-heart patient dies

The world's first twin-heart transplant patient has died, after living four months with a spare heart. The idea of giving a man a second heart was tried by Christiaan N. Barnard in Cape Town, South Africa, under the presumption that if something goes wrong with the new heart, it can be removed and "the patient is at least no worse off than when he started." The new technique, however, does not overcome the basic problem of the body's tending to reject transplanted foreign tissue (SN: 11/16/74, p. 314).

Ivan Taylor, 58, was suffering from terminal heart disease when he received his second heart last Nov. 25 (SN: 12/7/74, p. 358). No reason was given for his death on April 11. Another patient who received a second heart on New Year's Eve was reported doing well. In all, Barnard has given 14 patients new hearts. □

Charting ocean's profile from space

A satellite destined to be "the best-tracked spacecraft ever launched by the National Aeronautics and Space Administration" has been sent into an almost perfect orbit, from which it will provide data ranging from the height of ocean waves to the shape of the world.

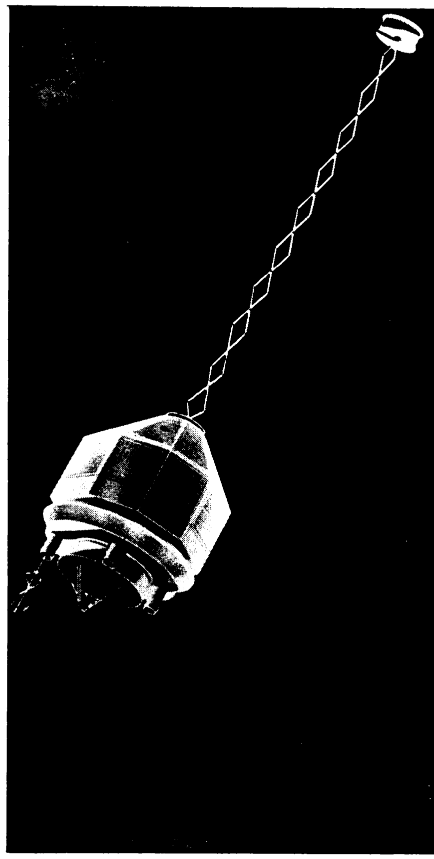
Known as GEOS-3, the third Geodynamics Experimental Ocean Satellite, launched last week, is the latest and most sophisticated in a line that goes all the way back to the second object ever put into orbit by the United States. Vanguard-1, launched March 17, 1958, made its mark by proving that the earth is not merely a flattened sphere, but pear-shaped. Since that time, satellite measurements of the shape, gravitational field and mass distribution of the planet have become increasingly precise, to the point where GEOS officials are talking about measuring the globe to within 10 centimeters.

Besides looking at the total planet, this latest GEOS is taking on a second task: mapping the ever-changing "topography" of the ocean. The primary instrument aboard the satellite is its ocean-watcher, a radar altimeter that bounces signals off the surface of the sea and times the echoes.

One purpose of such measurements is to refine the "ocean geoid," the shape that the ocean surface would follow in the absence of winds, currents and tides. GEOS-3's altitude reckonings are expected to be so precise that researchers plan to monitor ocean swells, waves and storms as part of a future goal of making regular "sea state" information available by satellite for shipping, weather forecasting and other applications.

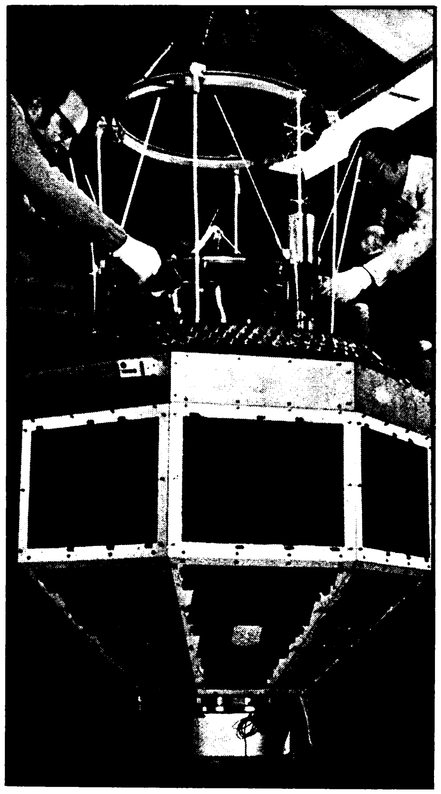
The prototype of the radar altimeter was one of the instruments aboard Skylab, as part of the manned space station's earth-resources experiment package. Data gathered during Skylab, in fact, are now being used to construct models of the sea surface for comparison with GEOS-3 results.

Wave-height measurements with 10-centimeter accuracy are not quite in GEOS-3's capability, although determinations to less than one meter may be possible. Even so, to make such measurements from the satellite's altitude of about 840 kilometers requires that the probe's height and position be known to the best obtainable accuracy. To do this, it will be tracked from the ground not only by the conventional radio doppler method, but by two kinds of radar, and even lasers. A triple ring of 264 specially shaped quartz reflectors girdling the satellite will reflect ground-



Johns Hopkins APL

Stabilizer positions GEOS-3 in orbit.



Shroud covers altimeter before launch.

based laser beams to yield accuracies as fine as 10 centimeters in the probe's position. Careful positioning of the reflectors, and studies of what happens to the beams when they strike the reflectors at varying angles, should pro-