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How does the lowly bacterium sense its environment? Cornell researchers discover lattice of supersensitive receptors

By Krishna Ramanujan

When humans taste or smell, receptors unique to each nerve cell detect the chemical and send signals to the brain, where many cells process the message to understand what we are smelling or tasting. But a bacterium is just a single cell, and it must use many different receptors to sense and interpret everything around it.



Kevin Stearns/University Photography

Cornell researchers who developed a model for how the complex of receptors in bacteria is organized include, from left, Professor Jack Freed, Assistant Professor Brian Crane, and Senior Research Associates Alexandrine Bilwes, seated, and Peter Borbat. Copyright © Cornell University

Bacteria can sense in their environments changes in molecular concentrations as small as 0.1 percent, the equivalent of one drop diluted in a pool of a 1,000 drops. How do they do it?

New Cornell research, highlighted on the cover of the May issue of *Nature Structural and Molecular Biology*, reveals that receptors assemble into a kind of cooperative lattice on a bacterium's surface to amplify infinitesimal changes in the environment and kick off processes that lead to specific responses within the cell.

"Bacteria sense a lot of different things. But assume it's a sugar molecule that a bacterium needs as a nutrient -- even a 0.1 percent change in concentration can be detected, and this sensitivity is maintained over five orders of magnitude in nutrient

concentration," said Brian Crane, assistant professor of chemistry and chemical biology and corresponding author of the paper. "Biologically, I know of no other system that is so sensitive over such a large range."

Crane believes the kind of cooperative lattice found in bacterial receptors may in fact point to a general mechanism for cellular signaling and serve as inspiration for developing molecular devices. Such devices could be used to sense a wide range of chemicals, light, ionic strength (salt), pH and heavy metals with great sensitivity, gain and dynamic range. Scientists are interested in developing synthetic systems with such sensing properties as well as engineering bacteria that respond to stimuli such as pollutants or explosives.

Using a combination of X-ray crystallography to determine the structure of receptors and enzymes and a novel spectroscopic technique for measuring interactions between them, Crane's group was able to develop a model for how the complex of receptors is organized. Jack Freed, Cornell professor of chemistry and chemical biology and director of the National Biomedical Center for Advanced ESR Studies at Cornell, developed the spectroscopic technique, called pulsed electron spin resonance dipolar spectroscopy.

The researchers suggest that when one receptor detects, for example, a sugar in its environment, communication of some sort triggers an array of linked receptors to rearrange itself, much like when water freezes, all the water molecules assort themselves into a new structure. Through

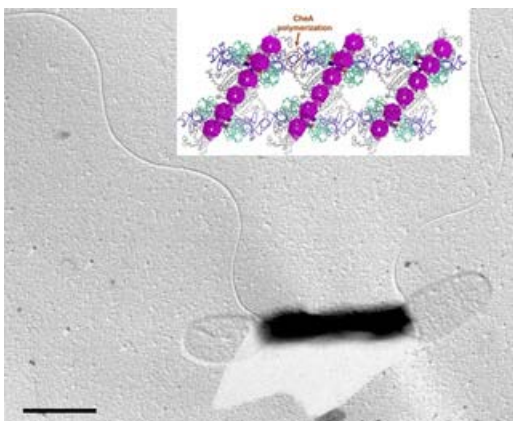


Image provided by Drs. Reinhard Rachel and Karl Stetter, University of Regensburg

Image from an electron microscope of *Thermotoga maritima* bacteria showing flagella projecting from each end of the cell. In the proposed structure of a cooperative lattice (as viewed from the membrane into the cell), rows of receptors are linked by enzymes (inset).

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this reorganization, the bacterium's receptor array amplifies the signal that a specific molecule has been sensed outside the cell. This structural shift then activates kinases, or enzymes, within the cell, starting a chain reaction that leads to a response, such as changing how the flagella (or tails) spin. This allows the bacterium to move toward or away from what it has sensed.

Such a mechanism of amplification allows signals from the receptors to travel hundreds of angstroms, a distance used in atomic physics that is a virtual marathon in the world of intracellular communication. Ten angstroms equal a nanometer, which is one-billionth of a meter.

Sang-Youn Park, a former graduate student in Cornell's Department of Chemistry and Chemical Biology, and senior research associates Peter Borbat and Alexandrine Bilwes were the study's lead authors. The research was funded by the National Institutes of Health.

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