Microbial study reveals sophisticated sensory response

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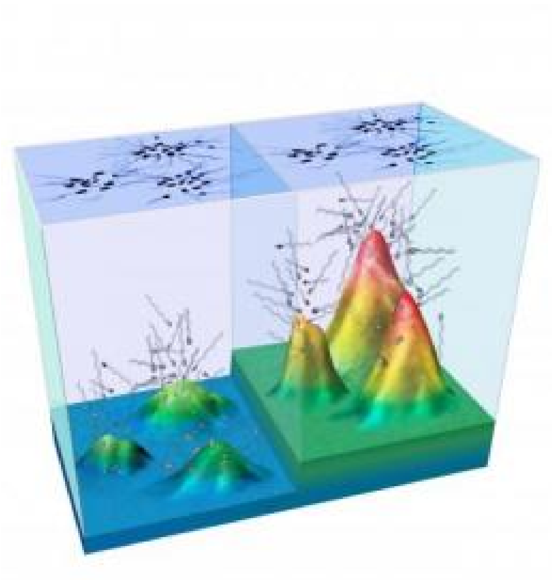

This artist's rendition shows bacteria executing a newly discovered mode of adaptive sensory response, called "fold-change detection." Researchers at AMOLF and MIT found that *Escherichia coli* bacteria respond identically when nutrient gradients (shown as colored landscapes) are rescaled by the same factor as the background concentration of nutrients to which they have adapted. Credit: Image / Bellomo, Shimizu, Gorick and Stocker

All known biological sensory systems, including the familiar examples of the five human senses – vision, hearing, smell, taste and touch – have one thing in common: when exposed to a sustained change in sensory input, the sense eventually acclimates and notices subsequent changes without continuing to compare each new change with the initial condition. This autonomous tuning of perceptions, known as sensory adaptation, has been recognized by scientists for more than a century, but a new study has demonstrated that even a simple microbe can achieve this feat with surprising sophistication.

In a paper appearing the week of August 1 in the *Proceedings of the National Academy of Sciences* online, researchers at the FOM Institute for Atomic and Molecular Physics (AMOLF) and the Massachusetts Institute of Technology (MIT) describe, for the first time, a biological system in which sensory adaptation is so precise that behavior remains identical even in ever-changing "background" conditions. The researchers' system of choice is the bacterium Escherichia coli; they studied how this microbe's sensing of food alters its swimming behavior, or chemotaxis.

The new research is a collaboration between a Dutch team led by AMOLF group leader Tom Shimizu and an MIT team led by Roman Stocker, a professor in the Department of Civil and Environmental Engineering. Other team members are Milena D. Lazova, a graduate student in biophysics at AMOLF who is lead author of the paper; Tanvir Ahmed, who completed his Ph.D. studies at MIT in June; and Domenico Bellomo, an electrical engineer and systems biologist at the Delft University of Technology.

"This bacterial system offers a unique opportunity in the study of biological sensory processes," Shimizu said. "Its simplicity allows us to connect the molecular mechanisms, responsible for signal reception and processing, directly to how the organism behaves."

Much as animals often depend on the sense of smell to find food, the microscopic bacteria — each a single cell measuring only 2-4 micrometers in length — rely on a chemical sensing system to locate nutrients. To characterize this sensory response, Shimizu's group took advantage of a physical phenomenon known as Förster resonance energy transfer (FRET) that allows the monitoring of molecular interactions inside living cells using optical measurements.

Stocker's group conducted experiments using microfluidic devices – fluid channels of microscopic dimensions that allow precise control over the physical and chemical environment — to characterize changes in the bacteria's chemotaxis. Both types of experiments showed that when the size of the gradients in nutrient abundance was increased or decreased by the same factor as the changes in the background level of nutrients, the bacteria responded identically.

Previous research had characterized the molecular machinery responsible for this microbe's sensory behavior, and how adaptation enhances the ability of bacteria to perform food searches under varied conditions. The new experiments demonstrate that the bacteria achieve this by a precise modulation of perception through sensory adaptation. This study is the first to show that a biological system responds only to the "fold change" in sensory inputs in a changing environment: instead of responding to the absolute magnitude of the chemical concentrations they encounter, they respond to relative changes (or the ratio of the stimulus size to the background level).

"Bacteria encounter a large spectrum of nutrient concentrations," said Stocker. "In the ocean, for example, micromolar and millimolar pulses of nutrients arising from cell deaths or excretions dot an otherwise nanomolar nutrient landscape. A sophisticated rescaling of chemotaxis, such as we found for *E. coli*, would provide a strong fitness advantage when foraging in these environments."

A novel aspect of the discovery is that this relative perception is achieved not just for instantaneous changes in the sensory input, but also for changes that occur gradually.

An example of an instantaneous change is a man walking into an unlit room and seeing only darkness until, after a few minutes, his eyes adjust and he's able to make out objects in the room. This adjustment allows the man to effectively ignore the background — or overall level of light — and instead focus on the "contrast," the change in light relative to the background, to construct the visual scene.

Now consider the man searching for his car keys in a scene with a more gradual change in light, for example, a wooded landscape. The overall brightness of the wooded scene can be considered the background level of sensory input and it will change as he moves through areas that are more densely or sparsely covered by trees. To search for his keys effectively, the man would again like to ignore the background, but this time it is changing continually as he walks. An efficient strategy under these conditions, it turns out, is responding to changes not relative to a fixed background, but rather to the input experienced at every moment in time.

Whether our own eyes can perform this dynamic fold-change detection as in the example above, has yet to be seen. But the new research shows that a simple microbe is capable of this sophisticated sensory behavior and also explains the underlying molecular machinery.

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