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The 'surprisingly simple' arithmetic of smell

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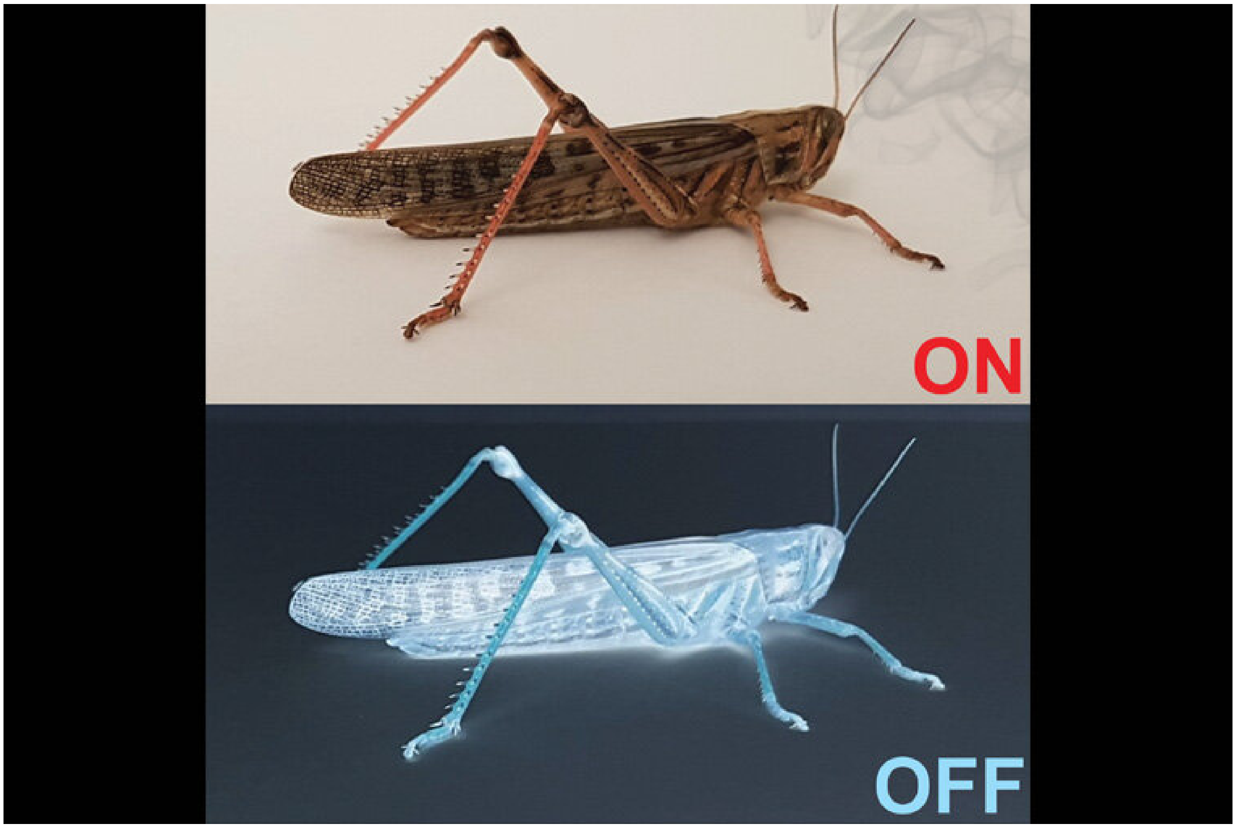

After reaching a threshold of ON neurons, a locust can smell an odor. Once OFF neurons fire, the smell goes away. Credit: Raman lab

Smell a cup of coffee.

Smell it inside or outside; summer or winter; in a coffee shop with a scone; in a pizza parlor with pepperoni—even at a pizza parlor with a scone!—coffee smells like coffee.

Why don't other smells or different environmental factors "get in the way," so to speak, of the experience of smelling individual odors? Researchers at the McKelvey School of Engineering at Washington University in St. Louis turned to their trusted research subject, the locust, to find out.

What they found was "surprisingly simple," according to Barani Raman, professor of biomedical engineering. Their results were published in the journal *Proceedings of the National Academy of Sciences* of the United States of America.

Raman and colleagues have been working with locusts for years, watching their brains and their behaviors related to smell in an attempt to engineer bomb-sniffing locusts. Along the way, they've made substantial gains when it comes to understanding the mechanisms at play when it comes to locusts' sense of smell.

To understand how it is that a locust can consistently recognize smells regardless of context, they took a cue from Ivan Pavlov. Like Pavlov's dogs, locusts were trained to associate an odor with food, their preference being a blade of grass. After going a day without food, a locust was exposed to a puff of odor (a puff of hexanol or isoamyl acetate), then given a blade of grass. In as few as six such presentations, the locust learned to open its palps (sensory appendages close to the mouth) in expectation of a snack after simply smelling the "training odorant." Just like us recognizing coffee, the trained locust could recognize the odor and did not let other factors get in the way.

At this point, researchers began looking at which neurons were firing when the locust was exposed to the odor under different conditions, including in conjunction with other smells, in humid or dry conditions, when they were starved or fully fed, trained or untrained, and for different amounts of time.

Under different circumstances, it turned out, researchers saw highly inconsistent patterns of neurons were activated even though the locust palps opened every time. "The neural responses were highly variable," Raman said. "That seemed to be at odds with what the locusts were doing, behaviorally."

How could variable neural responses produce consistent or stable behavior? To probe this, researchers turned to a machine-learning algorithm. "We wanted to see if given these variable neural response patterns, can we predict the locust behavior?" Raman said. "The answer was yes, we can."

The algorithm turned out to be very simple to interpret. It exploited two functional types of neurons: there are ON neurons, which are activated when an odorant is present, and there are OFF neurons, which are silenced when an odorant is present but become activated after the odor presentation ends.

"You can think of the ON neurons as conveying 'evidence for' an odor being present, and OFF neurons as 'evidence against' that odor being present," Raman said. To recognize an odorant's presence, researchers simply needed to add evidence for the odorant being present (i.e. add the spikes across all ON neurons) and subtract evidence against that odor being present (i.e. add the spikes across all OFF neurons). If the result was above a certain threshold, machine learning would predict the locust smelled the odor.

"We were surprised to find that this simple approach is all that was needed to robustly recognize an odorant," Raman said.

Raman likened the process to shopping for a shirt. Say you have a list of qualities you're looking for—cotton, long sleeves, button-down, solid color, maybe a front pocket to hold your glasses—and a few dealbreakers, such as dry-clean only or polka dots.

You may get lucky and find a shirt that is precisely what you are looking for. But, more pragmatically, you would make a purchase as long as many of the features you are looking for are present and the majority of features that are deal breakers are not present.

Finding the features you want is similar to the information conveyed by the ON neurons. Absence of deal breakers is similar to silencing of the OFF neurons. As long as enough ON neurons that are typically activated by an odorant have fired—and most OFF neurons have not—it would be a safe bet to predict that the locust will open its palps in anticipation of a grassy treat.

More information: Srinath Nizampatnam et al, Invariant odor recognition with ON–OFF neural ensembles, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2023340118

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