Tracking worm sex drive, neuron by neuron

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Jagan Srinivasan, PhD, assistant professor of biology and biotechnology at Worcester Polytechnic Institute (WPI). Credit: Worcester Polytechnic Institute

The males prowl a dark, crowded space. Using a mix of instinct and sensory cues, they pursue potential mates. But how do they decide when to make their move? New findings answer that question, at least for the tiny soil-dwelling worms known as *Caenorhabditis elegans* (*C. elegans*).

Research conducted at Worcester Polytechnic Institute (WPI) and California Institute of Technology (Caltech) has found that where and when a male worm will pursue a mate is determined by four male-specific sensory neurons that communicate with synaptic feedback loops to form a decision-making network. The team reports their findings in the paper "Contrasting responses within a single neuron class enable sex-specific attraction in *Caenorhabditis elegans*" published on Feb. 22, 2016, in the journal *Proceedings of the National Academy of Sciences.*

"With just four sensory neurons the male is able to make a sophisticated calculation about the concentration of certain pheromones that are secreted by other *C. elegans* seeking to attract a mate," said Jagan Srinivasan, PhD, assistant professor of biology and biotechnology at WPI and a corresponding author of the new paper. "The worm, essentially, calculates a derivative of the concentration curve and uses that information to decide where to move for the best chance at finding a suitable mate."

Noted Paul Sternberg, PhD, professor of biology at Caltech, Howard Hughes Medical Institute investigator, and co-corresponding author of the paper, "our data imply that we found not only the primary sensor for these sex pheromones, but also an apparently novel mechanism of neural coding to efficiently process information."

An adult *C. elegans* is about 1 millimeter long and has approximately 1,000 cells, about a third of which are dedicated to their nervous system. Despite its small size, the worm is a complex organism able to do all of the things animals must do to survive, including foraging for food and seeking out mates, making it one of the most powerful research models in molecular biology.

Most *C. elegans* worms are self-fertilizing hermaphrodites, carrying both egg and sperm cells. Male worms account for less than 1 percent of the population. As hermaphrodites deplete their sperm cells they secrete pheromones to attract males. A male worm must mate with a hermaphrodite to fulfill its evolutionary goal of passing along its genes to the next generation.

In the current study, researchers analyzed the electrical activity of four sensory neurons located near the male worm's head (two on each side). In a controlled environment, they released varying concentrations of the attractive pheromones and monitored the individual responses of the four neurons. Based on previous research in the field, Srinivasan and the team assumed the four anatomically identical neurons would respond the same way, at the same time, to the same environmental cues.

Surprisingly, the sensory neurons reacted in very different ways, and for different durations, depending on the concentration of the pheromones and the synaptic activity with other neurons. In some cases, a neuron would react quickly to the scent of the pheromone, and in other cases the same neuron would essentially turn off and stop sending sensory signals, even in the presence of a heavy concentration of pheromones.

"Our data suggests a strategy for pheromones, where the same set of four (neurons) encode different concentrations in excitatory and inhibitory responses...," the authors wrote. "Encoding different concentrations within a single neuronal class appears to be another method by which nematodes, with their compact nervous system, break symmetry to increase coding capacity," allowing the worm to glean more information from its environment than if the neurons simply switched off and on.

The team also found that the level of synaptic activity, meaning the communication between neurons, was related to the worm's decision to move toward a scent. In healthy worms, this sensory circuit led most of the worms toward an intermediate concentration of the pheromones, not the strongest concentration. High concentrations of the pheromones can indicate overcrowding or other stresses in the environment that make it less conducive to successful mating, the authors noted. Conversely, a small concentration of the scent would mean too few hermaphrodites were nearby to justify moving in that direction. When the team disabled three of the four sensory neurons, or purposely decreased the overall the level of synaptic activity, those worms with just one functional sensory neuron no longer showed a preference and instead moved directly towards any concentration of the pheromone.

"For the intact worm, there is an optimal concentration of the pheromones, and that can differ from one worm to another," Srinivasan said. "You can think of it as a personal preference. It's not just a matter of following any scent, or the strongest concentration."

This newly observed circuit likely involves molecules called neurotransmitters that need to be further characterized, Srinivasan said. "This opens up many new questions to explore, and we expect that some of the neurotransmitters involved may play a role in the human brain."

More information: Anusha Narayan et al. Contrasting responses within a single neuron class enable sex-specific attraction in Caenorhabditis elegans, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1600786113

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