

Worm-tracking challenge leads to new tool for brain research

October 3 2011

Using new optical equipment, a team of 11 researchers put roundworms into a world of virtual reality, monitored both their behavior and brain activity and gained unexpected information on how the organism's brain operates as it moves.

The new research tracking system -- created in collaboration with Eugene-based Applied Scientific Instrumentation Inc. (ASI) -- should help neuroscientists around the world who use other small organisms, such as <u>fruit flies</u> and <u>zebra fish</u>, in their studies to understand how the <u>central nervous system</u> is tied to behavior, said Shawn R. Lockery, professor of biology and director of the Institute of Neuroscience at the University of Oregon.

In a paper in the online journal <u>PLoS ONE</u>, a publication of the Public Library of Science, researchers detail how the dual camera tool works and how they used it in experiments with freely moving roundworms (<u>Caenorhabditis elegans</u>).

The research team, led by Serge Faumont, a senior research associate in the Institute of Neuroscience, found that certain neurons remain active as roundworms move forward and backward. Researchers had theorized that some neurons would be active when moving forward and then shut down as another set of neurons engaged when the animal reversed.

This basic-level research provides a window in which scientists can explore links between the brain and behavior, how <u>neuronal activity</u>



might be organized and how <u>genetic mutations</u> may affect connections more broadly, such as in mental illness in humans, Faumont and Lockery said.

"We want to understand the physical basis of thinking, in particular of consciousness," Lockery said. "But we don't have access to another person's or animal's thoughts directly. The only access we have is through behavior."

The roundworm-human connection is genetically strong, Faumont noted. "Sixty percent of the genome of *C-elegans* is conserved in humans," he said. "You can knock out a gene in a worm, and know that that gene has a human version."

"Studies like this, with this nematode, which has only 302 neurons and about 5,000 synapses," Lockery said, "are important because biologists have repeatedly discovered that evolution is conservative -- that there are very strong relationships in terms of molecules and mechanisms, including those in the brain, between simple organisms and humans."

Using simple organisms, he said, allows researchers to potentially gain a complete understanding of a brain, "whereas we may never fully understand the human brain." Gaining insights on where modularity exists -- and where it breaks down -- provides fundamental insights that can guide researchers studying the brains of more complicated animals, Lockery said.

The device allowed roundworms, specially bred with neurons containing fluorescence, to move about freely and naturally on a specially lubricated platform in an environment watched over by cameras that keep the animals centered -- and all of their <u>brain activity</u> and movements recordable. That is the magic of the system, Lockery said. Keeping the target sites fully centered and constantly observable to catch all



complexities had been a barrier, Faumont said.

"Imagine looking at a squirrel with a pair of powerful binoculars, and all you can see is an eye," Faumont said. "You are trying to keep the eye of the squirrel centered while the squirrel is doing an activity and jumping around. This represents a complex tracking problem."

The sensitive microscopy device created by Lockery's lab and ASI keeps the roundworms' fluorescently lit neurons centered in a constant field-ofview and monitored as they move about at speeds of up to 500 microns, or about one-half millimeter a second. Two specialty cameras -- based on ASI's Phototrack system -- provide for synchronized viewing and recording that captures simultaneously neuronal activity and behavior.

In the team's virtual reality experiment, roundworms were placed in an environment in which a blue laser would trigger an avoidance response in <u>neurons</u> known to react to a perceived toxin, by recoiling or reversing to avoid danger. In the absence of the blue light, animals moved freely. "This experiment provides proof-of-concept for creating high-resolution virtual environments for exploring the neuronal control of behavior in freely crawling organisms," the team wrote.

Lockery approached ASI, which was founded in 1990, about the tracking challenge during an international <u>neuroscience</u> meeting in 2006. The ensuing collaboration resulted in a highly sensitive tracking system that ASI owns and that Lockery's lab gets to use and help improve. The company manufactures electro-mechanical devices that are used around the world by cell biologists, neuroscientists, pharmaceutical companies and material scientists.

Neither Lockery nor the University of Oregon holds a financial interest in the device. "This has been a perfect collaboration between industry and academic research," Lockery said. Such collaborations, said study co-



author Gary Rondeau, ASI's technical director, help to keep ASI on the cutting edge for new product development.

"We are frequently asked to look at new special applications," Rondeau said. "This keeps the work fresh and aimed at the constantly changing needs of our customers in the research community. Some projects, like this one, are just fun. It's nice to use our talents to develop new ways to achieve scientific goals that haven't been possible before. Talking over details of experiments with creative researchers such as Shawn and Serge is always stimulating, and then seeing things come together is very satisfying."

Provided by University of Oregon

Citation: Worm-tracking challenge leads to new tool for brain research (2011, October 3) retrieved 4 May 2024 from https://medicalxpress.com/news/2011-10-worm-tracking-tool-brain.html

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