

Caltech, UC Berkeley to Investigate How Brain Activity Controls Complex Behavior

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A new \$4.4-million grant from the National Science Foundation will allow researchers at the California Institute of Technology and the University of California, Berkeley, to develop techniques to turn brain cells on and off in animals as they go about their daily activities, allowing the scientists to understand the details of how brain activity leads to complex behaviors.

According to principal investigator Michael Dickinson, the Zarem Professor of Bioengineering at Caltech, the five-year program is aimed at solving one of the remaining great challenges facing biologists--understanding the mechanistic basis of complex behavior. The work will focus on fruit flies, which are a powerful model system understood extremely well at the genetic level.

"New approaches available in molecular genetics can now be applied to manipulate individual brain cells in an attempt to understand how brains control behavior," says Dickinson. "We'll also use recent advances in engineering to create new devices to observe and measure behavioral changes in a manner as rigorous as those available to detect genetic differences."

The work will involve experiments in which the activity of specific cells in the nervous systems of fruit flies can be controlled using light. "The idea is to bioengineer ion channels that can be opened and closed with light flashes," Dickinson explains. "By controlling these genetically engineered ion channels, we can directly manipulate the electrical

impulses that nervous systems use to sense and process information.

"This approach will allow us to study the function of specific cells and circuits in intact animals," Dickinson adds. Coinvestigator Ehud Isacoff of the University of California, Berkeley, will create these ion channels.

A fly might be engineered, for example, to begin flying or walking when pulsed with light of a certain wavelength. But this would be a means to a scientific goal and not the ultimate goal itself.

"This is one way of tapping into the fly and making cells do what we want them to do in order to test specific hypotheses about brain structure and behavior," Dickinson says. David Anderson, a coprincipal investigator and the Sperry Professor of Biology at Caltech, will work to place the light-controlled ion channels within as many unique cells in the flies' nervous systems as possible.

Prior work on the cellular basis of behavior has focused on how networks of brain cells may control simple behaviors such as swimming, flying, and feeding. The new work will probe these behaviors at a deeper level, attempting to figure out how nervous systems-and possibly even individual nervous-system cells-regulate simpler motor actions over time and space to generate more complex behaviors.

A central goal of the research will be to determine how a nervous system uses sensory data to process changes in a complex set of behaviors. Thus, the scientists will not only study the details of how the flies' sensory-based locomotion (walking and flying) works, but how their locomotion is related to crucial survival activities such as looking for food, seeking mates, laying eggs, searching for shelter, and getting out of harm's way.

"We will begin with the assumption that an animal's own natural behavior is the best context in which to interpret how its nervous system

is built," Dickinson says. "The first step is to gather quantitative behavioral information concerning the external and internal cues that cause flies to change or modulate what they are doing.

"The next step is to gain experimental access to the specific cells that control these behavioral transitions, so we will develop genetically engineered flies that allow us to control the neurons that send information from the sensory areas of the brain to the circuits that generate and control movement. We will also study how gene expression controls and alters brain wiring.

"Collectively, this may help unravel one of the central questions in neuroscience: how brains regulate behavioral transitions."

Source: Caltech

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