3-D map of fly brain is to neuroscience what genome is to genetics

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In an advance that is being compared to the sequencing of the fly genome, researchers have created the first brain-wide wiring map of a fruit fly. The breakthrough paves the way for a comprehensive analysis of information processing within and between neurons and ultimately a deeper understanding of control and causality in fly behavior, according to the researchers who report their findings online on December 2 in *Current Biology*.

"Our finding opens up a systematic way to understand how the brain functions," said lead author of the study Ann-Shyn Chiang of National Tsing Hua University in Taiwan. "It is the brain map equivalent of sequencing the genome."

"In my view, this work is very exciting and comparable to the fly genome in setting a new benchmark in biology," said Ralph Greenspan of the University of California, San Diego, who was not involved with the study. "It tells us succinctly how a complex brain is put together, and given the ever-increasing evidence for conservation of the genetic programs underlying neuronal development and function, it probably tells us at a smaller scale what the human brain will also look like."

The researchers constructed the map using what they call a reverse-engineering approach. They deconstructed a fly brain into thousands of single neurons (representing about 10 percent of the neurons in the entire fly brain) and then put them back together into a common standardized framework to produce a virtual fly brain. The resulting three-

dimensional map offers a view of the basic units of information processing and the major "traffic" patterns that flow through them.

That 3D diagram of neural networks shows that the fruit fly brain consists of families of information-processing units linked by tracts. Specifically, the researchers identified 41 local processing units (LPUs), 6 hubs, and 58 tracts covering the whole fly brain.

"Each unit is like a city containing local intersected streets and avenues linked to other cities through multilane highways without cross-traffic," Chiang said. "Sometimes, several geographically closed units form a family working together for a specific function requiring intensive information processing."

In computer terms, Chiang says, the results reveal the fly brain as a hybrid system of distributed computing, with most processors loosely coupled and geographically dispersed, and clustered computing, with some processors clustered for specific functions. "It seems that a fly brain is smarter and more complicated than any computer built thus far," he said.

The researchers have made their findings available to the scientific community through an open-access image database called FlyCircuit (http://www.flycircuit.tw) for online data archiving, mining, analysis, and 3D visualization of all single neurons, brain-wide LPUs, their wiring diagrams, and neural tracts. Researchers can use the new database and tools to generate hypotheses and guide genetic manipulations aimed at understanding how genes and circuits orchestrate complex behaviors. They can also use FlyCircuit to upload and analyze their own data.

"Similar to genomics sequencing data for understanding gene functions, the discovery-based FlyCircuit repository of 3D images of single neurons is a hypothesis-generating resource for understanding brain

functions," Chiang said.

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