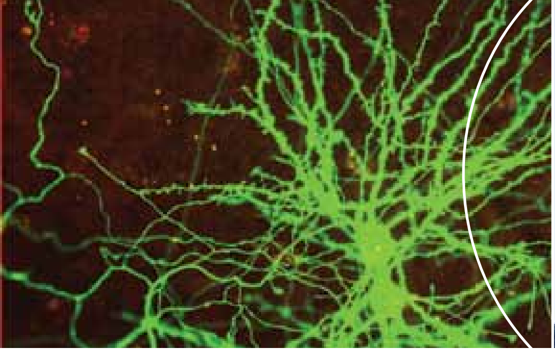

Edward M. Callaway

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"Our brain performs millions of complex computations every second. We are studying the organization and function of neural circuits in the visual cortex to better understand how specific neural components contribute to the computations that give rise to visual perception and to elucidate the basic neural mechanisms that underlie cortical function."

Neuroscientists have identified dozens of different neuronal cell types in the brain that work together in distinct networks. But the circuits are intermingled, and even neighboring neurons of the same type differ in connectivity and function. Without access to a "wiring diagram"—a map of the neuronal connections—attempting to grasp how the brain lets us understand language, recognize faces, and schedule our day is akin to trying to discern how a computer chip works simply by looking at it.

Recently, Callaway and his team of researchers have jumped what many believe to be a major hurdle to preparing that diagram: figuring out single connections between neurons. They successfully modified the rabies virus, turning it into a tool that can cross the synaptic space of an infected nerve cell just once to identify all the neurons to which it reaches out. Viruses that naturally spread between neurons have previously been used to outline the flow of nerve cell communication, but without a way to stop them in their tracks, over time, they will light up the whole brain.

Callaway's team deleted a gene required by the virus to spread across synapses, marooning the virus inside a cell. Supplying the missing gene in that same cell, however, allowed the virus to slip into all the cells that were directly connected to it. Since these neighboring cells lacked the gene supplied in the first cell, the virus was now permanently stuck. To restrict the viral infection to a certain cell type or even to single cells, they festooned these neurons with avian surface molecules and equipped the rabies virus with a homing device specifically for neurons "disguised" as bird cells.

While the first, published experiments were conducted using slices of brain, more recent studies are using transgenic mice to allow targeting of a specific class of neurons. The rabies virus then identifies the inputs to just that one neuron class. With these tools, the wiring map can then be constructed step by step as subsequent populations of cells are visualized. And once scientists can identify a neural circuit, they can then correlate it with such brain functions as perception and behavior.

For more information, please visit
salk.edu/faculty/callaway.html

Left to right:
Fumitaka Osakada, James Marshel, Patrick Chan, Ali Cetin, Karine von Bochmann, Mauricio de la Parra, Andrea Hasenstaub, Ed Callaway, Al Kaye, Hendrikje Nienborg, Hoang Nhan, Stephani Otte, Marina Garrett