Unraveling fine-scale and cell-type specificity of cortical circuits

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We have studied primary visual cortex to better understand how neural circuits give rise to perception. We have found that cortical circuits are extremely precise, such that different neuron types, and even neighboring neurons of the same type, are connected differently. For example, different types of inhibitory neurons with overlapping dendritic arbors receive connections from different cortical layers. And neighboring excitatory neurons only receive common input from the same presynaptic neurons in the minority of cases when they are directly connected to each other. This fine-scale and cell type-specific organization implies that studies of relationships between circuits and function should match this level of organization. To test hypotheses about contributions of specific cell types to neuronal responses and to perception, we have developed methods to allow reversible inactivation of selected cell types. We find that expression of an insect neuropeptide receptor which couples to GIRK channels can be used to selectively, quickly, and reversibly eliminate the activity of neurons in vivo. This methods allows tests of the role of particular cell types within the intact, functioning neural network. To allow the circuitry of specific neurons to be more directly linked to function we have developed a method that allows the neurons directly presynaptic to a single neuron to be labeled genetically. This method is compatible with functional characterization of the postsynaptic neuron and future development should also allow functional characterization of the presynaptic cells by expression of genetically encoded activity sensors.