NEUROANATOMY

Mapping neural function alongside connectivity

A detailed understanding of neuronal circuits will require the ability to combine knowledge of neuronal anatomy and activity. Now, two studies provide a first step in this direction by demonstrating that neural function can be integrated with network connectivity through a combination of functional imaging and serial electron microscopy.

In the first study, Briggman *et al.* investigated the functional connectivity of direction-selective ganglion cells (DSGCs) and starburst amacrine cells (SACs) in the mouse retina to provide insight into the underlying mechanisms of motion direction computation.

DSGCs are activated by certain directions of motion, with different cells responding optimally to different directions of movement. Furthermore, these neurons fail to respond to motion oriented at 180° to the preferred direction of motion, the so-called null direction. SACs also respond to motion — various dendrites in individual SACs respond to different directions of motion

— and form inhibitory synapses onto DSGCs.

To achieve the study's objective, Briggman *et al.* first conducted two-photon calcium imaging on a mouse retina exposed to moving-bar stimuli, to identify the direction selectivity of the various DSGCs. Subsequently, they performed serial block-face electron microscopy on the functionally imaged tissue to establish local network connectivity.

The authors found that SAC dendrites that were oriented at 180° to the preferred directions of the DSGCs tended to selectively form synapses with these cells. This finding, therefore, supports the long-debated hypothesis that the asymmetrical direction selectivity of DSGCs is largely conferred by SAC-derived lateral inhibition of DSGCs during null-direction movement.

Evidence from several previous physiological studies suggested that in the visual cortex, inhibitory interneurons were less responsive to stimulus orientation than were pyramidal cells. In a second recently

published study, Bock *et al.* explored the basis of this differential sensitivity, testing the hypothesis that inhibitory interneurons in the mouse visual cortex received convergent inputs from excitatory pyramidal neurons with varying preferences in stimulus orientation.

The authors presented black and white bars to an anaesthetized mouse, and simultaneously conducted two-photon calcium imaging of a group of cells in the primary visual cortex to assess stimulus orientation preferences. Subsequently, they performed serial-section transmission electron microscopy on these cells and reconstructed the neuronal network's connectivity.

The authors noted that on multiple occasions, several pyramidal cells with differing preferences in stimulus orientation provided convergent input to one inhibitory interneuron. Interestingly, further analysis revealed that between pairs of pyramidal cells, axon-to-axon proximity was a more reliable predictor of input convergence than was orientation preference.

Taken together, these results indicate that inhibitory interneurons in the visual cortex are, at most, weakly tuned to the orientation of visual stimuli, and suggest that these cells have a supportive role in visual computations, perhaps through the provision of inhibitory feedback to pyramidal cells to sharpen selectivity responses.

The new studies show how the operation of neuronal networks can begin to be addressed through functional imaging performed in tandem with large-scale electron microscopy.

Darran Yates

ORIGINAL RESEARCH PAPERS Briggman, K. L., Helmstaedter, M. & Denk, W. Wiring specificity in the direction-selectivity circuit of the retina. *Nature* **471**, 183–188 (2011) | Bock, D. D. *et al.* Network anatomy and in vivo physiology of visual cortical neurons. *Nature* **471**, 177–182 (2011)