in the local field potential. By injecting repeating patterns of excitatory and inhibitory conductances into pyramidal neurons — matching the characteristics of excitation and inhibition during actual UP states — the authors showed that inhibition is important in determining the timing and probability of action potential generation.

This study builds on previous findings to show that inhibitory interneurons can control the precise timing of action potentials in postsynaptic cells, thereby driving cortical network synchronization. In this way, inhibitory networks direct the flow of information in the neocortex.

Rebecca Craven

References and links

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AXON GUIDANCE

Axon development branches out

New work by Portera-Cailliau and colleagues, using *in vivo* two-photon time-lapse imaging, sheds light on some of the intricacies of axonal development and shows distinct patterns of structural and dynamic change according to cell type.

These researchers imaged axonal growth and pruning in transgenic mice that express green fluorescent protein in two types of axon in layer 1 of the neocortex: long-distance axonal projections of thalamocortical neurons and local axons of Cajal–Retzius interneurons. Imaging took place in the first 3 weeks of postnatal development, during which time both of these neuronal types elaborate and mature.

There were several striking differences in the progression of elaboration between the two types of cell, despite their identical environment. In the first week, thalamocortical axons had small growth cones that typically lacked filopodia, and had only a few long branches. After this stage, the branches appeared more rapidly and were shorter. Eventually, the axons became more complex and stable. At all imaging time points, thalamocortical axons tended to grow along relatively straight paths.

By contrast, in the first week, the growth cones of Cajal–Retzius axons were large and had many long filopodia. At this point, the axons had many branches and branch tips were still growing, but the rate of addition of new branches declined during and after the first week, and was lower across all time points than for thalamocortical axons. These axons also followed more convoluted routes than thalamocortical axons.

Axons are generally thought to undergo a stage of axonal overgrowth followed by pruning. However, contrary to this view, Portera-Cailliau and colleagues found that, for both long projection neurons and interneurons, individual axonal arbors grew and retracted simultaneously at different branch tips. These processes were most pronounced during the first week of postnatal development and were more rapid in the case of thalamocortical axons. Growth occurred to only a marginally greater extent than retraction.

Interestingly, these authors observed two types of axonal pruning taking place over different length scales: retractions of short branch tip segments in both cell

A single thalamocortical arbor in layer 1 of the neocortex at postnatal days 8, 11, 13 and 17. Note that some branches are added whereas others are eliminated over time. Images courtesy of C. Portera-Cailliau, Department of Neurology, University of California, Los Angeles, California, USA.

types and, surprisingly, degeneration of large portions of thalamocortical axonal arbors, which disintegrated into tiny debris. Similar fragments were also seen in control mice, which indicates that this is a normal developmental process and not an effect of the surgery or *in vivo* imaging.

The mechanism by which branches form is the subject of some debate. Three possible mechanisms have been proposed: the splitting of growth cones, delayed growth cone branching and interstitial branching, whereby branches develop from new growth cones anywhere along the main axon shaft. These authors found evidence in favour of interstitial branch formation in both axonal subtypes, thereby helping to resolve this controversy.

This work provides a detailed picture of early axonal development and suggests that different cell types rely on different strategies of elaboration to innervate their target cells in identical environments. Future research might reveal the different mechanisms involved and identify the factors that determine which axon tips grow and which retract, and those that lead to axonal degeneration.

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