CORTICAL NETWORKS

Getting the timing right

Networks of inhibitory interneurons could be largely responsible for the propagation of higher-frequency activity in the cortex, concludes a new report from David McCormick's laboratory.

Most synapses onto neurons in the neocortex are supplied by other cortical neurons, forming 'recurrent' or 'feedback' networks. The encoding of information in cortical networks depends on the firing rate of individual neurons and on the temporal precision and relative timing of action potentials between neurons. Cortical networks can generate activity at a wide range of frequencies, but although slow, sleep-related oscillations have been studied in some detail, little is known about the production of higher-frequency cortical oscillations.

Hasenstaub *et al.* looked at spontaneously occurring recurrent network activity in the ferret dorsal prefrontal cortex. They recorded postsynaptic potentials or currents from cortical pyramidal neurons, showing that GABA$_A$ (γ-aminobutyric acid type A) receptor-mediated inhibition is required for the higher-frequency components of network-driven synaptic activity.

During periods of recurrent network activity (so-called UP states), inhibitory postsynaptic potentials carried more power than excitatory potentials at frequencies above 10 Hz, particularly in the gamma (30–80 Hz) frequency range, and were more synchronized. Fast-spiking inhibitory interneurons discharged strongly during UP states, and a robust relationship was detected between the discharge probability of these cells and the phase of the gamma oscillation

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HEARING

Hitting the right pitch

Two studies — one in monkeys and one in humans — have recently shed light on how primates perceive the pitch of a sound. Pitch perception is essential for appreciating music or fully understanding speech, but its neural basis is unclear.

The pitch of a sound, which can contain many different frequencies (harmonics), is related to its fundamental frequency (f_0). Complex sounds with very different frequency spectra can have the same pitch if their fundamental frequency is the same — even if the fundamental frequency itself is missing from the sound, leaving just the higher harmonics. However, neurons in the early stages of the auditory system tend to respond to simpler physical properties of a sound, such as frequency, rather than to subjective characteristics, such as pitch.

In the first study, Bendor and Wang used electrophysiological recordings from the marmoset cortex to look for neurons that responded specifically to the pitch of a sound. They found an area in the auditory cortex, close to the border of the primary auditory cortex, where neurons responded to sounds of a particular pitch — regardless of whether the sound was a pure tone or a complex sound with a missing fundamental frequency. The location of these neurons was consistent with areas that have been identified as pitch-sensitive in imaging studies of the human brain.

The second study involved the use of psychophysical techniques to divide participants into two groups: those who use the implied (missing) fundamental frequency of a complex sound to identify its pitch, and those who instead rely on the spectral envelope of the sound. Schneider *et al.* then investigated the neural substrate of pitch perception in these two groups with structural MRI scans and magnetoencephalography. In particular, they looked at the structure and function of an area of cortex known as Heschl's gyrus, which has previously been implicated in pitch perception.

Participants who used spectral information to determine pitch tended to have a greater volume of grey matter in the lateral Heschl's gyrus of their right hemisphere than the left, whereas the opposite was true for those who relied on the implied fundamental frequency. Consistent with this asymmetry, the participants who based pitch perception on spectral envelope also showed greater activity on the right side than the left, and again the opposite occurred in those who used fundamental frequency. These findings are in line with studies in which the left hemisphere has been found to be specialized for processing rapid temporal information, whereas the right hemisphere has been implicated in spectral processing.

These insights into how pitch is represented in the cortex are important advances, even though there is still much to be learned about the neuronal processing and representation of pitch.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPERS Bendor, D. & Wang, X. The neuronal representation of pitch in primate auditory cortex. *Nature* **436**, 1161–1165 (2005) | Schneider, P. *et al.* Structural and functional asymmetry of lateral Heschl's gyrus reflects pitch perception preference. *Nature Neurosci.* **8**, 1241–1247 (2005)

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

ORIGINAL RESEARCH PAPER Hasenstaub, A. *et al.* Inhibitory postsynaptic potentials carry synchronized frequency information in active cortical networks. *Neuron* **47**, 423–435 (2005)

FURTHER READING Shu, Y. *et al.* Turning on and off recurrent balanced cortical activity. *Nature* **423**, 288–293 (2003)

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.

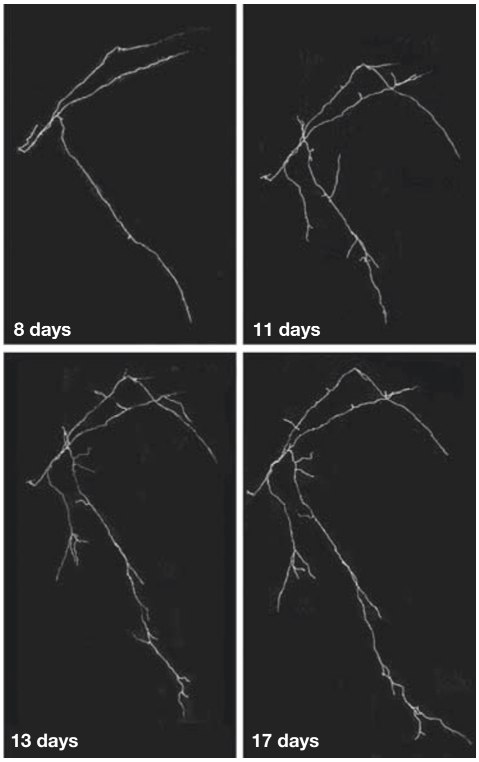
These researchers imaged axonal growth and pruning in transgenic mice that express green fluorescent protein in two types of axon in layer 1 of the neocortex: long-distance axonal projections of thalamocortical neurons and local axons of Cajal–Retzius interneurons. Imaging took place in the first 3 weeks 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 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.



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.

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.

Alison Rowan

References and links

ORIGINAL RESEARCH PAPER Portera-Cailliau, C. *et al.* Diverse modes of axon elaboration in the developing neocortex. *PLoS Biol.* **3**, e272 (2005)