NEUROANATOMY

Reach out and touch

Dendritic spines are a popular subject these days. One theory is that they exist, at least in part, to allow axons to synapse with dendrites without deviating from a nice straight path through the brain. But, as Anderson and Martin point out in *Nature Neuroscience*, axons can also form spine-like structures, known as *terminaux* boutons. Might these also be used to maintain economic, straight axonal trajectories?

Anderson and Martin proposed that, if this were the case, the two types of axonal connection — *terminaux* boutons and *en passant* boutons — would each make synapses preferentially with different types of dendritic site. *Terminaux* boutons would be used to 'reach out' to dendritic shafts, whereas *en passant* boutons (where synapses are formed on the shaft of the axon) would occur when dendritic spines were able to bridge the gap between dendrite and axon. They carried out a detailed morphological study of spiny neuron axons in cat cortex to test this hypothesis.

Perhaps surprisingly, they found that the two types of synaptic bouton did not differentiate between dendritic spines and shafts. Axons were just as likely to use *terminaux* boutons to contact dendritic spines as they were to use *en passant* boutons, even in cases where it would seem that the path of the axon would allow it to use an *en passant* bouton. So, why do axons bother to construct these delicate structures, if not simply to connect to out-of-the-way dendrites?

NEURAL CODING

A barrel of spikes

Sensory events, at least in complex nervous systems like ours, are encoded by neuronal populations rather than individual neurons. It has been difficult to determine exactly what features of neural firing — spike timing or spike counts, independent spikes or patterns — are used to carry information. A recent study by Petersen *et al.* concludes that, in rat somatosensory cortex at least, the timing of the first spikes from single neurons in response to a stimulus is the crucial element for coding stimulus location.

The 'barrel' cortex in the rat lends itself well to analysis because of its relatively simple and stereotyped organization. The cortex is divided into columnar barrels, each of which receives input primarily from a particular whisker. In addition, the neurons in the barrels tend to fire low numbers of spikes, simplifying the task of analysing the population code.

Petersen *et al.* recorded from pairs of neurons in barrel cortex while they stimulated individual whiskers. They then quantified the roles of different elements of the population activity in encoding stimulus location by evaluating the proportion of available information that was carried by each element. They found that most of the signal — around 85% — was contained in the timing of the individual spikes, especially the first spike fired by each neuron after the stimulus. The rest of the information was carried by spike patterns within neurons.

The authors tested whether patterns of spikes in the population activity reflected redundant or synergistic coding by comparing the information conveyed by the population as a whole with that conveyed by individual spikes. Within a cortical barrel, coding was redundant. This might seem to be inefficient, but the authors point out that it could provide useful robustness, and allow the same information to be transmitted simultaneously to different targets. Between columns, on the other hand, pairs of neurons code independently.

One important question is, if first-spike time is so important, how can the animal use it? After all, the experimenter knows exactly when the stimulus occurred, but the animal doesn't. One possible explanation lies in the active nature of the somatosensory system in rats under normal circumstances. When exploring an environment, a rat will use its whiskers to collect information by sweeping them backwards and forwards, and it could use a copy of the motor command to predict when the stimulus was likely to have occurred. In addition, the sensory system could use the relative times of first spikes between columns, rather than the absolute timing in a single column, to encode location. Barrel neurons respond to their preferred whisker with a short latency, but they also respond more weakly and with a longer latency to neighbouring whiskers, so comparing the times at which neurons in neighbouring barrels fire could provide the relevant information. The two techniques could even be combined for greater precision.

As analytical and recording techniques are improved, it should be possible to apply this kind of analysis to more complex systems and more natural, dynamic stimulus sets. Understanding how the nervous system codes and decodes its messages is one of the great challenges for neuroscientists today, and this kind of study takes us closer to that goal.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Petersen, R. S. *et al.* Population coding of stimulus location in rat somatosensory cortex. *Neuron* **32**, 503–514 (2001)

FURTHER READING Pouget, A. *et al.* Information processing with population codes. *Nature Rev. Neurosci.* **1**, 125–132 (2000)

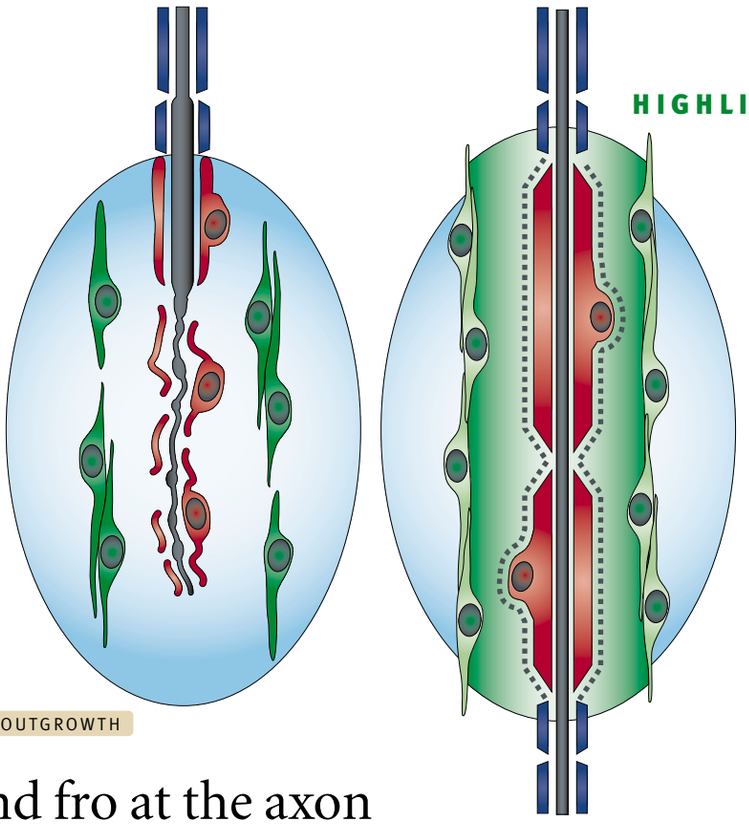
The authors propose that *terminaux* boutons might share some of the physiological properties of dendritic spines. For example, spines are known to compartmentalize calcium transients. If these axonal structures also prevent calcium from diffusing rapidly into the parent axon during an action potential, *terminaux* boutons might show more presynaptic facilitation than *en passant* boutons. Of course, there is no evidence yet that *terminaux* boutons have this kind of influence on synaptic dynamics and plasticity, but the demonstration that they seem not to be simple bridges does compel us to consider alternative functions.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Anderson, J. C. & Martin, K. A. C. Does bouton morphology optimize axon length? *Nature Neurosci.* 19 November 2001 (10.1038/nn772)

FURTHER READING Hering, H. & Sheng, M. Dendritic spines: structure, dynamics and regulation. *Nature Rev. Neurosci.* **2**, 880–888 (2001)



PROCESS OUTGROWTH

To and fro at the axon

Cut an axon and it will probably regress. This form of axonal death is commonly termed Wallerian degeneration, and although it was originally described many years ago, its underlying mechanisms have not been explored in detail. Part of the reason for this neglect is the simple assumption that retraction of the severed axon is merely a passive process. It was therefore surprising to discover a mutant mouse — the c57BL/*Wld*^{S} strain — in which Wallerian degeneration did not occur. What protected the axons of these mice from degeneration? Until recently, we did not know much about this mutation, other than that it was related to a triplication of the so-called *Wld*^{S} region of mouse chromosome 4. This region harbors a chimeric gene that is formed by a small fraction of the coding region of ubiquitination factor E4B and a gene termed *D4Cole1e*, the function of which was so far unknown. But now Mack *et al.* have obtained evidence that *D4Cole1e* is the mouse homologue of *NMNAT*, a human gene that encodes a key enzyme in the synthesis of NAD$^+$. They also showed that overexpression of the chimeric gene protects axons from Wallerian degeneration.

Expressing *Ube4b/Nmnat* in transgenic mice had a dose-dependent protective effect against Wallerian degeneration. Although the chimeric protein did show NMNAT activity, the relationship of this enzymatic action to the protective mechanism is not clear; the protein was found largely in the nucleus and the cellular content of NAD$^+$ did not increase in the transgenic animals. However, the results constitute solid evidence that *Ube4b/Nmnat* is responsible for the *Wld*^{S} phenotype, and rule out the contribution of other genes that are present in the triplicated region.

But not every axon dies after injury. If the axon is not severed but crushed, it can sometimes regenerate and function normally. The regeneration process requires the deployment of cellular resources, such as the synthesis of new proteins. Owing to the paucity of ribosomes in axons, it was commonly believed that the cell body orchestrated the recovery response. However, Zheng *et al.* now report that regenerating axons can locally synthesize proteins, even if they are excommunicated from the soma.

The authors isolated regenerating sensory axons and showed that they contained β-actin and neurofilament mRNAs bound to ribosomes. Moreover, they found evidence for protein synthesis in this preparation, and showed that blocking translation caused retraction, but only if the axon was separated from the cell body. This finding indicated that axonal protein synthesis might contribute to regeneration only if the supply of proteins from the cell body is compromised. But more importantly, the data of Zheng *et al.* constitute some of the best available evidence that protein synthesis can occur in axons, and not only in somata and dendrites, as we have long assumed.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPERS Mack, T. G. A. *et al*. Wallerian degeneration of injured axons and synapses is delayed by a *Ube4b/Nmnat* chimeric gene. *Nature Neurosci.* **4**, 1199–1206 (2001) | Zheng, J.-Q. *et al*. A functional role for intra-axonal protein synthesis during axonal regeneration from adult sensory neurons. *J. Neurosci.* **21**, 9291–9303 (2001)

FURTHER READING Conforti, L. *et al*. A Ufd2/D4Cole1e chimeric protein and overexpression of *Rbp7* in the slow Wallerian degeneration (*Wld*^{S}) mouse. *Proc. Natl Acad. Sci. USA* **97**, 9985–9990 (2000) | Twiss, J. L. *et al*. Translational control of ribosomal protein L4 is required for rapid neurite extension. *Neurobiol. Dis.* **7**, 416–428 (2000)