replace cations in the lattice framework with cations that have a lower positive charge. For example, when cobalt ions (Co^{2+}) substitute for some of the aluminium ions (Al^{3+}) in aluminophosphates, a porous solid is generated that catalyses oxidations[4]. Such cation substitutions result in a framework that has an overall negative charge. This can be balanced by placing cations in the nanoporous channels. If reactive cations are used, this is a second way to activate catalytic behaviour.

A breakthrough in zeolite science came with the discovery that previously unknown structures could be made by adding organic bases to the chemical reactions used to prepare zeolites[5]. These organic bases seem to act as a template for the formation of micropores and are now commonly used in zeolite synthesis, although the molecular details of their role are poorly understood.

Now, Weckhuysen and colleagues[1,2] have advanced our understanding of the molecular mechanism for the organic-base-mediated synthesis of zeolites. Zeolites usually form as gels, which then crystallize into the desired microporous solids. The authors used a combination of *in situ* techniques to examine this crystallization process. They applied X-ray scattering methods[1] previously also used to study silicalite synthesis from solution[6] to probe the dimensions of particle aggregates and the presence of crystals. They combined this with spectroscopy[2] to investigate the local environment of the atoms.

Weckhuysen and colleagues compared the formation of the chargeless $AlPO_4$-5 framework with the negatively charged framework (known as ZnAPO-34) that is formed by replacing aluminium ions in $AlPO_4$-5 with zinc ions (Zn^{2+}). The authors followed not only the structural changes in the aluminophosphate gel in real time, but also the conformational features of the organic base (tetraethylammonium hydroxide) used as a template for the crystallization. The tetraethylammonium cation adopts one of two conformations once it takes up its position in the aluminophosphate nanopores.

The authors prepared the ZnAPO-34 structure, which contains spherical cavities rather than channels, simply by adding zinc ions to the aluminophosphate gel. They also made similar structures by adding either cobalt ions (Co^{2+}) or manganese ions (Mn^{2+}) to the gel[2], showing that the influence of dipositive cations on the lattice topology is general. Their studies revealed previously unknown details of the crystallization process — for example, particles of crystalline material, about 11.5 nanometres in size, initially form in the ZnAPO-34 gel before increasing in size[1]. Most intriguingly, not only do ZnO_4 tetrahedra form in the recursor gel before crystallization begins, but the tetraethylammonium ion also adopts the conformation that it will ultimately assume in the crystal. In the case where no zinc is present and $AlPO_4$-5 forms, the organic template takes on the alternative conformation.

These results[1,2] are highly relevant to the debate on the mechanism of zeolite formation and the role of organic base molecules[6–9]. The implication is that the tetraethylammonium ion forms a complex with developing zeolite subunits in the gel (Fig. 1), adopting a molecular structure close to that found in the final crystal[2]. This molecular recognition process determines which type of crystal lattice is formed. For ZnAPO-34, the distinctive spherical cavities of the crystal may actually form first in the gel, forcing the tetraethylammonium ion into the conformation seen in the solid. The near absence of this conformation in the alternative $AlPO_4$-5 system corroborates this theory. Furthermore, Weckhuysen and colleagues' data are in line with proposals on the mechanism of silicalite formation from its synthesis solution[6,9]. It is thought that precursor nanoparticles of silicalite might appear before crystallization, and that these nanoparticles are aggregates of complexes formed between SiO_4 units and the organic base used in the reaction.

Weckhuysen and colleagues[1,2] have thus shed light on the mechanism of zeolite formation, providing experimental support for the idea that molecular organization occurs before crystallization. The insights obtained from this work will certainly benefit the search for the next generation of microporous materials. More generally, the authors' powerful combination of analytical techniques will enable the physical chemistry of many other synthetic processes to be monitored *in situ*, so that the structural changes involved can be observed as they happen. ■

Rutger A. van Santen is at the Schuit Institute of Catalysis, Eindhoven University of Technology, Box 513, 5600 MB Eindhoven, The Netherlands.
e-mail: r.a.v.santen@tue.nl

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NEUROBIOLOGY

Crossed circuits

Andrew B. Schwartz

Can the brain be induced to reroute neural information? Such an achievement is crucial if the function of damaged brain areas is to be taken on elsewhere. A study in monkeys explores this prospect.

The rapidly growing field of neural engineering has led to the development of electronic devices that interact directly with neurons, with the aim of examining fundamental neural operations and of replacing damaged brain functions. In work described on page 56 of this issue, Jackson, Mavoori and Fetz[1] use a self-contained electronic circuit implanted in the brains of monkeys to demonstrate a basic feature of learning — the ability to change the routing of neural information — that could prove useful in rehabilitative therapy.

The authors used off-the-shelf components to build what they call a Neurochip. Neurons in the brain's motor cortex fire impulses during voluntary movements, and the Neurochip picks up these impulses, or 'spikes', by means of a recording microelectrode placed near the neurons. Through the Neurochip, the spikes trigger an electric-stimulus pulse through a second, stimulating electrode at an adjacent site in the motor cortex. Because the circuit is self-contained, this spike–stimulus sequence could be carried out continuously for 24 hours while the animal went about its normal activities in its cage (termed the conditioning period). The idea behind the Neurochip was that, by picking up the signals from one neuronal circuit and transferring them to another repeatedly over a 24-hour period, a new information route might be formed. This would have obvious potential with regard to rehabilitation after neural injury, but it would also give insight into learning, which is thought to occur as neural circuits and connections are strengthened through use.

The authors also used a technique called intracortical microstimulation (ICMS), which provides a measure of neural connectivity[2,3] between the cortical neurons and muscles, to assess whether the neural circuit had been rerouted by the Neurochip during the conditioning period. In ICMS, high-frequency bursts — or trains — of electrical pulses (in the range 10–100 microamps) are passed through microelectrodes in the cortex, activating a large network of neuronal connections spanning the cortex, subcortical structures and the spinal cord to generate muscle twitches.

Cortical neurons that project to different muscles are in fact intermixed in the part of the motor cortex that is likely to be activated by ICMS[4]. Because of the extent of this network, it is not possible to delineate a specific functional route between the stimulation site and the observed muscle twitch using ICMS by itself, and it is difficult to ascribe a specific causal role to any cortical neuron. But although ICMS is only a rough measure of connectivity, it can indicate when the pathways change in response to external stimuli. For instance, activation of the muscles by ICMS changes rapidly with peripheral-nerve injury[5], or even when a limb is placed in a splint for just a few hours[6].

Fetz and colleagues[1] used ICMS before the conditioning period to define the direction of force produced at the wrist when they stimulated the motor cortex around the Neurochip recording and stimulation sites (Fig. 1). A combination of muscles was probably activated from each ICMS site, and different combinations produced different force directions. ICMS applied at the recording site generated torque in one direction, whereas that applied at the stimulating site generated torque in another. The Neurochip was then used to apply single shocks at the stimulation site each time a spike occurred at the recording site during the conditioning period.

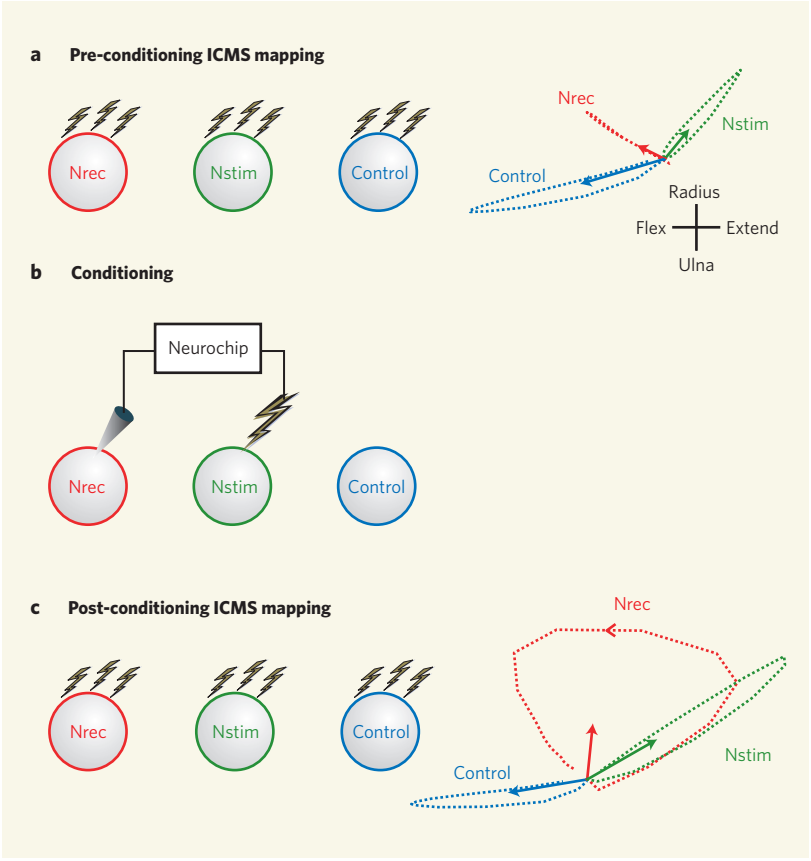

Figure 1 | Reorganizing a neural circuit. Fetz *et al.*[1] implanted a 'Neurochip', which had a recording microelectrode (Nrec) and a stimulating microelectrode (Nstim), in the motor cortex of a monkey. **a**, Using a technique called intracortical microstimulation (ICMS), they passed a series of electric pulses into the cortex next to the two Neurochip electrodes and at a control region to map the muscle responses at the monkey's wrist. The right panel shows the wrist torque produced by ICMS, with the arrows showing the mean trajectory. **b**, The next step was a conditioning period, when the Neurochip recorded the activity of a single neuron in the cortex. Every time there was an activity spike in that neuron, the Neurochip sent an electrical pulse through the stimulating microelectrode into another neuron. **c**, After 24 hours of conditioning, the ICMS response was measured again. The response produced by ICMS near the Neurochip recording site had changed towards that produced near the Neurochip stimulation site, showing that the neural circuit had been partially rerouted by conditioning.

When ICMS was applied to the recording site after this conditioning period, the torque direction produced at the wrist had changed, becoming more like that produced by the stimulation site (a shift from flexion towards radial deviation). So it seems that a change may have occurred in the network between the recording site and the muscle. The authors suggest that connectivity is enhanced between the recording and stimulation sites, and that this is facilitated by horizontal connections in the motor cortex, but that is just one possibility. ICMS induces many neurons to fire in relation to one another, in ways that may not happen during normal behaviour. But the authors also used an alternative technique that measures the correlation of spiking between pairs of neurons or between a neuron and muscle, avoiding the complication of artificial connectivity. So far, these data show a clear correlation only between activity in the single neuron being recorded and the two opposing antagonist muscles in the wrist. If the horizontal-connectivity hypothesis is correct, then further studies should show that ongoing spike activity at the two electrode sites is more correlated after conditioning. In addition, spikes recorded at the recording site should show an increased cross-correlation to the activity patterns (EMG) of muscles that are correlated to the stimulation-site activity.

The results show clearly that stimulation at a particular cortical location activates pathways to multiple muscles, and that the conditioning procedure may change the effective bias of these pathways. Whether this is facilitated by local connections between neurons in the cortex, or through more remote projections to, for example, subcortical and spinal structures, is still an open question. The predominant pathways descending to the musculature from the motor cortex have many neuronal junctions, with nerve fibres projecting to other cortical regions, the thalamus, subcortical structures, and throughout the intermediate layers of the spinal cord. Even the few fibres that end directly on motor units in the spinal cord facilitate contraction in a variety of muscles that generate torque in different directions. The pairing strategy used by Fetz and colleagues[1] is likely to alter the connections throughout this extensive network, changing the muscle bias elicited from the ICMS site. This explanation is supported by the finding[1] that the 20-millisecond delay of the stimulus following the conditioning trigger spike has an optimal effect (merely changing horizontal connections in the motor cortex would generally require a conduction delay of only about 2 milliseconds).

Nonetheless, these effects observed by Fetz and colleagues are specific and long-lasting (persisting for more than a week after conditioning), warranting further experiments using similar technology in primates. Such neural devices, and the new research they spawn, will help to elucidate how the brain can change and adapt within the complexity of an intact nervous system, and will undoubtedly change our view of how learning occurs in higher-order species, including our own. ■

Andrew B. Schwartz is in the Departments of Neurobiology, Bioengineering and Physical Medicine and Rehabilitation, University of Pittsburgh School of Medicine, E1440 BST, 200 Lothrope Street, Pittsburgh, Pennsylvania 15213, USA.
e-mail: abs21+@pitt.edu

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