element is studied. Druitt and co-workers[1] measured the chemical gradients of magnesium across individual zones in feldspar crystals. Magnesium diffuses distances of about 10 micrometres a year at temperatures of 855 °C, and so is ideal for investigating processes that happen on timescales of centuries or less. The authors used the chemical gradients of the very slow-diffusing trace elements strontium and titanium to establish that the crystal zones they studied have a thermal origin, resulting from the addition of hotter magmas to the reservoir. They propose that a significant volume of this hot magma was added in one or more spurts during the decades or months that preceded the Minoan eruption. Each spurt would have generated vigorous seismic activity and considerable inflation of the island's surface, probably serving as harbingers of catastrophe for Santorini's Minoan inhabitants[3].

This short timescale between recharge of the reservoir with hot magma and subsequent eruption, compared with the 18,000-year period of dormancy between the Minoan eruption and the previous caldera-forming eruption at Santorini, echoes the short lead-in time previously calculated[4] for the much smaller 1925–28 lava eruptions on Nea Kameni island in the centre of Santorini's caldera (Fig. 1). The net pre-Minoan influx rate of hot magma calculated by Druitt *et al.*[1] is in excess of 0.05 $km^3\ yr^{-1}$, some 50 times greater than the long-term average rate at Santorini. This is consistent with an emerging consensus that assembly of magma reservoirs is piecemeal and pulsatory, and may accelerate before eruption. These pulses can potentially be modelled from real-time ground deformation[2]. The magnitude of deformation depends on the depth and shape of the magma reservoir, the size of the pulses, and how the heated rocks above the magma reservoir deform.

Santorini seems to be a volcano of habit. The island has seen two major cycles of magmatic activity, each lasting about 180,000 years and culminating in two large caldera-forming eruptions of silica-rich rhyodacite magma about 20,000 years apart; the Minoan is the most recent of these[5]. The early stages of volcanic activity in each cycle were marked by much smaller eruptions of magma that was more silica-poor (dacites, andesites and basalts). Since at least 197 BC, Santorini's caldera has been refilling with dacite lavas and the products of associated minor explosive eruptions[5]; the most recent lava eruption was on Nea Kameni in 1950. These lavas bear chemical similarities to the hotter magmas that flooded the magma reservoir before the Minoan eruption[1]. It is not clear whether they herald the start of a new eruptive cycle on Santorini or are vestiges of the last one.

Since early 2011, there have been increasing numbers of small earthquakes beneath the floor of the Santorini caldera[6], several centimetres of surface uplift[7] and increased release of magmatic carbon dioxide from the ground[8]. So far it is not certain whether these are the signs of an impending eruption — which would probably produce a dacite lava flow similar to the small, post-Minoan eruptions on Nea Kameni — or the usual restlessness that characterizes many dormant volcanoes. The difficult task facing those charged with monitoring Santorini[6] is interpreting the ongoing signs of unrest in the context of the most likely magmatic and tectonic processes responsible and the long-term behaviour of the volcano. Applications of diffusion chronometry to volcanic rocks from Santorini[1,4] provide valuable insight into the magnitude and timing of subterranean magmatic events that preceded previous eruptions both large and small. ■

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NEUROSCIENCE

Reward alters specific connections

How does the brain couple a fleeting sensory input to a delayed reward during learning? A study in locusts shows that coincident firing of neurons can 'mark' a neuronal connection for later modulation. SEE ARTICLE P.47

TIMOTHY E. HOLY

A whiff of food followed by a tasty meal can trigger a specific learned association. In the quest to explain learning mechanistically, a long-standing hypothesis known as Hebb's rule[1,2] posits that the pairing of stimulus and reward causes their respective neurons to be simultaneously active, and that this synchronous activity then changes the strength of the connections — synapses — between the neurons. But when stimulus and reward are not simultaneous, how does the brain pick the right synapses to modify? On page 47 of this issue, Cassenaer and Laurent[3] report that correlated neuronal activity, when followed by delivery of a neurotransmitter molecule known to be released by reward, changes synapses in distinctive ways in the locust olfactory system. Moreover, the authors observed these changes in live insects and using natural stimuli (odours).

The relevance of Hebb's rule in associative learning received significant experimental support with the discovery of long-term potentiation[4], in which coincident firing of two interconnected neurons results in a stronger connection between them. However, perhaps the clearest correlate of associative learning came much later, with the discovery of spike-timing-dependent plasticity (STDP)[5]. In this process, the firing (voltage spikes) of the pre- and postsynaptic neurons must occur within a few tens of milliseconds for synaptic change (plasticity) to occur.

STDP has been extensively studied and is widespread in the brain. However, any attempt to explicitly relate this cellular phenomenon to behavioural learning faces numerous obstacles. A simplistic view specifies that the presynaptic neurons should be stimulus responsive, and the postsynaptic neurons reward responsive. However, one must acknowledge that a dizzyingly large number of arbitrary stimuli can be associated with a tiny number of intrinsic rewards. Moreover, Hebb's rule requires that all possible connections are initially present so that they might be strengthened or weakened through experience. The result might be a 'reward bottleneck', in which numerous stimulus-responsive neurons compete with each other for wiring space and/or influence over a few reward-responsive neurons.

A second obstacle arises because neurons in the brain display ongoing 'spontaneous' activity, and accidental coincidences between the spikes of pre- and postsynaptic neurons would also trigger plasticity. So, the robustness of synaptic change must be considered in light of this 'noise' problem. The narrow time window for STDP reduces the likelihood of accidental coincidence, but the sheer number of connections made by typical presynaptic

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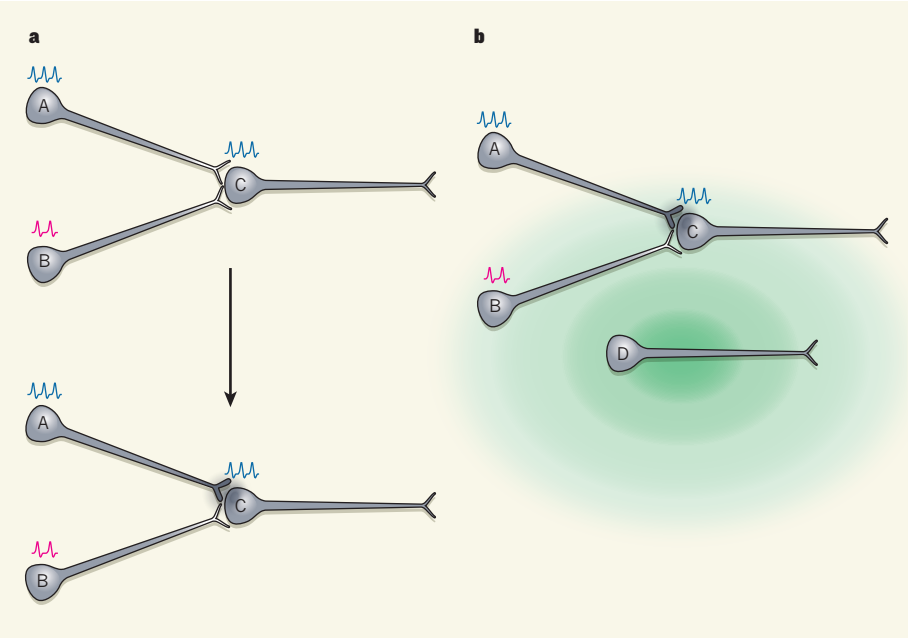

Figure 1 | Modulation of neuronal connections. Cassenaer and Laurent[3] observed synaptic modulation in a specific circuit of the olfactory system of live locusts. A and B represent neurons known as Kenyon cells, and C is a neuron from another part of the brain, the β-lobe. **a**, The strength of the synaptic connection between A and C changes when both cells fire repeatedly (blue spikes) within tens of milliseconds of each other. This process, known as spike-timing-dependent plasticity (STDP), may underlie some forms of associative learning in other systems, especially if stimulus and reward are simultaneous and are sensed by neurons such as A and C. The connection between B and C, by contrast, is not altered because they do not fire coincidently (red and blue spikes). **b**, STDP alone, however, cannot explain how stimulus and reward are connected when they occur hundreds of milliseconds apart. A possible missing link may be neuromodulatory transmitters (green) that are secreted by certain neurons (such as the reward-responsive neuron D) throughout the brain. The authors[3] show that one of these molecules, octopamine, can specifically weaken the synapses (such as the A–C synapse) that had been 'marked' 1 second earlier by STDP.

neurons seems to suggest[6] that random events are too common for reliable and stable learning through STDP alone.

A third problem is that the time window of STDP is too short to explain the seconds-long delays between stimulus and reward in typical associative-learning experiments. In some cases, sustained activity of presynaptic neurons[7] may circumvent this delay issue, but there are examples for which this does not seem to be the case. A particularly relevant example is found in the insect olfactory system, in which a group of neurons called Kenyon cells, residing in a part of the brain known as the mushroom body, respond to odours too transiently for their response to coincide with the delayed delivery of reward[8].

For the above and other reasons, researchers have focused on additional factors that regulate synaptic plasticity. Among the most prominent examples are neuromodulatory transmitters, such as acetylcholine, serotonin, dopamine, noradrenaline and octopamine. These molecules can increase or decrease the strength of synapses, and are therefore attractive candidates for mediating plasticity and learning. In both vertebrates and invertebrates, a modest number of modulatory neurons release these transmitters throughout the brain. By making reward-coupled signals widely available without the requirement for direct synapses onto reward-activated neurons, this architecture seems to relieve the reward bottleneck. However, it also implies that neuromodulators themselves cannot encode specific experiences. An attractive solution would be an interaction between neuromodulators and a synapse-specific process such as STDP. Indeed, numerous *in vitro* studies have revealed that the two do interact[9], but data on the relevance of these interactions *in vivo*, using natural sensory input, seem to be scarce.

Enter Cassenaer and Laurent[3]. Using live locusts as model organisms, they studied the synapses between the Kenyon cells and a small collection of neurons located in another part of the brain, the β-lobe. Unlike the sparsely firing Kenyon cells, β-lobe neurons fire in response to nearly every odour presented to the insect. By inserting tiny wires into the locust brain, the authors could stimulate different Kenyon cells with precise timing and record the corresponding inputs received by particular β-lobe neurons. Those synapses in which the inputs paired with the spikes of the β-lobe neuron became stronger or weaker in a typical STDP fashion (Fig. 1a).

In insects, the most well-studied mediator of reward is octopamine, and receptors for this neurotransmitter are abundant in the β-lobe[10,11]. To mimic associative-learning experiments (in which there is a delay between stimulus and reward), the authors[3] delivered a brief injection of octopamine one second after spike pairing. They found that this neurotransmitter dramatically changed how STDP worked: the synapse invariably became weaker, even under conditions in which it would normally have grown stronger. That is, plasticity still depended on precise temporal pairing of pre- and postsynaptic activity, but the addition of octopamine altered the outcome (Fig. 1b). The researchers obtained similar results when they used odour delivery, instead of electrical stimulation, to stimulate Kenyon cells.

These changes can be considered associative only if they are specific to the particular sensory experience paired with reward. In a beautiful final experiment, Cassenaer and Laurent[3] presented different odours sequentially to the locust, occasionally pairing one of them with octopamine injection. Whereas the neuronal responses to unpaired odours were scarcely affected by the neurotransmitter, the response to the paired odour was markedly decreased. Consequently, plasticity depended on the conjunction of odour-triggered activity and octopamine. It is worth noting that noradrenaline, an octopamine-related molecule, also changes olfactory circuitry in mammals and can trigger learning when paired with an odour[12,13]. Cassenaer and Laurent reveal the interaction of synapse-specific coincident firing and nonspecific neuromodulation — a combination that may help to resolve some major challenges to Hebbian plasticity, especially the delay problem.

Given the inherent complexities in relating brain-circuit processes to behavioural learning, many questions remain. One fundamental issue is whether octopamine resolves the noise problem of accidental coincidence. Indeed, over the short timescales of Cassenaer and Laurent's experiments[3], octopamine-modulated STDP was not obviously stronger, more quickly induced or more persistent than classical STDP. How, then, does (rare) neuromodulatory STDP overcome or overwhelm (common) ongoing STDP? The authors argue that, under normal conditions, ongoing STDP is balanced by mutually inhibitory activities of postsynaptic neurons, and so it requires new conditions — such as the presence of octopamine — to produce changes in neuronal firing. However, in the face of ongoing STDP, can such changes persist for long? These and similar questions will surely be tackled in future chapters of the long and complex story of memory. ■

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SURFACE CHEMISTRY

Crystal cuts on the nanoscale

A simple method has been developed to control the shape of nanoscale cuprous oxide crystals. Some shapes turn out to be much better than others as catalysts for a light-activated reaction.

PEIDONG YANG

The most popular diamond cut is the 'modern round brilliant', in which a gem is hewn to expose a specific set of crystal facets so as to produce exceptional brilliance. The arrangement of the facets is crucial for providing the maximum light return through the top of the diamond. It is becoming increasingly clear that crystal shape at the nanometre scale is similarly important for getting the best performance from solid catalysts. Writing in the *Journal of the American Chemical Society*, Huang *et al.*[1] report a beautiful example of how the specific crystal facets on nanoparticles of a material affect the catalytic properties of the particles in light-activated reactions.

Cuprous oxide (Cu_2O) has commonly been used as a pigment, a fungicide and an antifouling agent for marine paints. More recently, it has been reintroduced as a promising material for the cathode of photoelectrochemical cells, which use sunlight to split water into hydrogen and oxygen[2]. Huang *et al.*[1] have discovered a simple process for controllably synthesizing cuprous oxide nanocrystals as cubes, rhombic dodecahedra (polyhedra with 12 rhombic faces) and a variety of geometries in between (Fig. 1). The rhombic dodecahedra expose only one kind of facet (known in crystallographic jargon as {110} facets), and the authors observed that these nanocrystals are exceptionally good catalysts for the light-induced degradation of the organic compound methyl orange. This reaction serves as a model for reactions involved in clearing organic pollutants from the environment.

One of the tricks often used to control which shapes and facets form during the synthesis of nanocrystals is to preferentially adsorb certain molecular species to specific planes of atoms exposed on crystal surfaces. This strategy generates direction-dependent nanocrystal growth by stabilizing a particular facet — growth is limited on crystal planes where adsorption (and so stabilization) is strong, but is promoted on planes where adsorption is weak. A wide variety of chemical species can facilitate shape control in the growth of metal and oxide nanocrystals, including: surfactants, polymers and biomolecules; small molecules such as those in gases; and even atomic species, such as anions or metal ions.

It has previously been reported[3] that the shape of cuprous oxide nanocrystals can be controlled by varying the ratio of chloride ions to sodium dodecyl sulphate ions in the solutions from which the crystals form; the chloride ions stabilize the {100} planes of the crystals, whereas the dodecyl sulphate ions stabilize the {111} planes. In this way, a range of nanoscale polyhedra has been produced.

To make their cuprous oxide nanocrystals, Huang *et al.*[1] used a different recipe from that previously reported[3], and found that, by simply adjusting the amount of the reducing agent in the reaction mixture, they could control the shapes of the crystals. Their approach allowed them to make an alternative series of polyhedra (Fig. 1) to that produced in the earlier work. In addition, their shape-control method can be used at room temperature, unlike many previously reported strategies, which typically require higher temperatures.

Different nanocrystal shapes naturally display crystallographically distinct facets. In the absence of any major surface reconstruction processes, each facet type contains surface

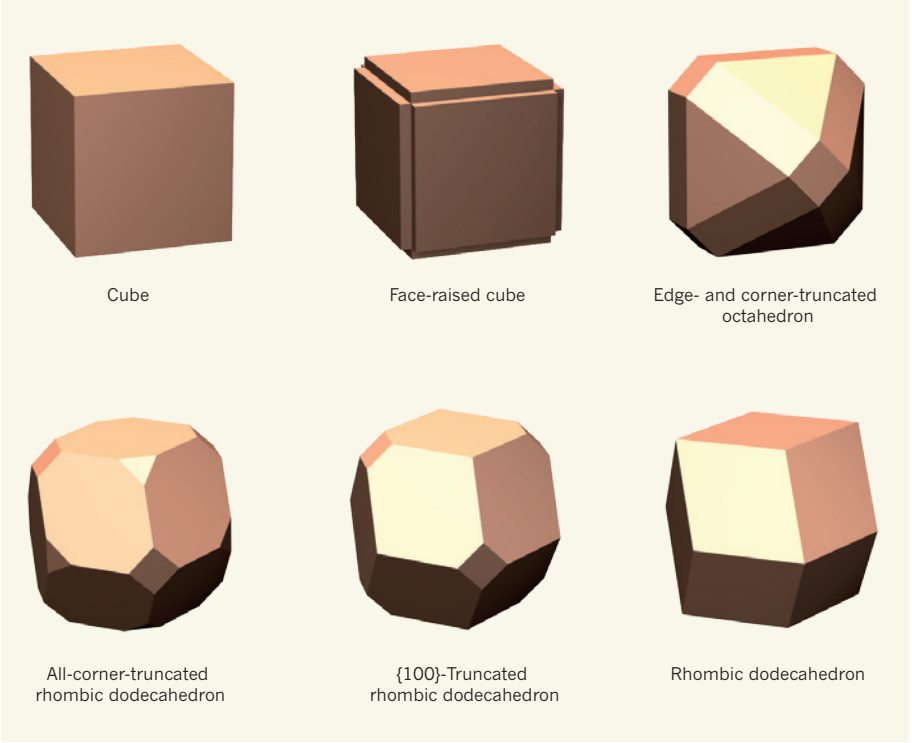

Figure 1 | Nanocrystal shapes. Huang *et al.*[1] report a simple process for controlling the shape of cuprous oxide nanocrystals during synthesis; the shapes made are depicted. The authors observed that the catalytic properties of the nanocrystals in a light-activated reaction — the degradation of methyl orange — largely depend on the kind of facets that the crystals have. Cubic crystals are essentially inactive, octahedra are moderately active, and rhombic dodecahedra are exceptionally active.

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