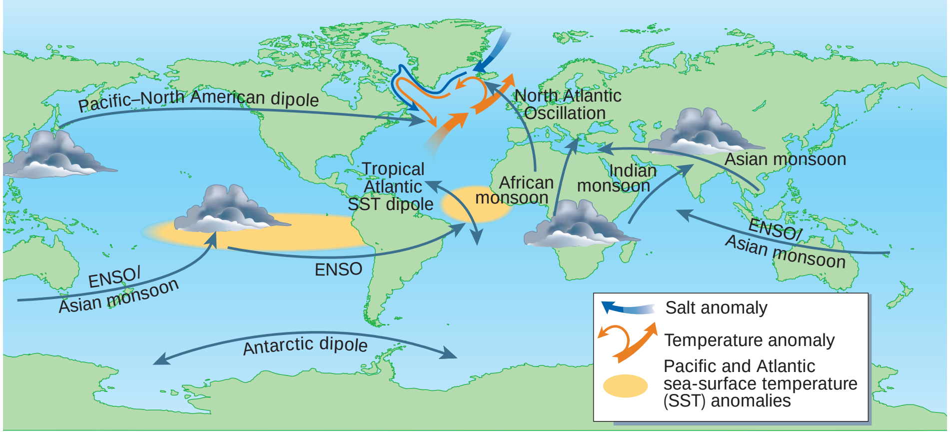
Box 1 Ocean–atmosphere teleconnections

Climate oscillators and dipoles interact in an intricate dance that redistributes moisture and heat in space and time across the globe. The monsoon subsystems — the Asian, Indian and African monsoons — are connected to variation in sea-surface temperatures in the Pacific. These, in turn, are linked to the El Niño Southern Oscillation (ENSO), so imposing a quasi ENSO-type pattern on monsoon precipitation. The pan-tropical ENSO influences high-latitude atmospheric dipoles, such as the North Atlantic Oscillation and the Antarctic dipole, which respectively determine precipitation patterns in the North Atlantic region and Eurasia, and the extent of sea ice around Antarctica. Together with the Pacific–North American dipole, the North Atlantic Oscillation constitutes the circum-Arctic wave. The Antarctic dipole is the quasi-stationary component of the circum-Antarctic wave.

Some of the heat stored in the tropical oceans, and transported to the poles in surface ocean currents, is released to the atmosphere and creates pressure anomalies. These cause changes in atmospheric convection patterns, and in levels of storminess and precipitation. In the North Atlantic, salinity anomalies are caused sporadically by bursts of fresh water from the Arctic Ocean and the Canadian Arctic seas, in conjunction with swings in the North Atlantic Oscillation. The salt anomalies stabilize the upper water column and affect oceanic convection patterns, with consequences for the North Atlantic as a source of heat and moisture to the atmosphere. Anomalies in the sea-surface temperature in the North Atlantic are connected with pulses in the transport of warm water in the Gulf Stream, that in turn show linkage with ENSO events in the Pacific. The sea-surface temperature anomalies feed back into the North Atlantic Oscillation, thereby stimulating changes in wind trajectories and precipitation patterns in the wider North Atlantic region. This then affects the strength of westerly winds into Eurasia, and snow accumulation there, which feeds into Asian monsoon activity.

These teleconnections are evidently highly complicated. We require a better understanding of how they differ in different climatic regimes, and how their stability is affected by changing boundary conditions. One especially large uncertainty is how variations in solar irradiance influence and alter climatic regimes. **R.Z.**



That belief is now long dead[12,13], and because of both natural and human-induced change we face an uncertain climate future. It will require a concerted effort from those involved in the observational, modelling and palaeoclimate aspects of climate change to integrate knowledge of the various climatic regimes, past and present, to assess the 'teleconnections' between them, and the stability of their links through time. Only then will we be able to forecast with any confidence potentially hazardous states of climate regimes[14,15] — for instance, certain anomalies in sea-surface temperatures in the Pacific and North Atlantic that might promote conditions in which severe flooding occurs in monsoon regions. In providing a more detailed view of monsoon variability in the recent past, and its teleconnections, Gupta and colleagues' contribution is a good example of how further progress can be made on this subject. ■

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Neurobiology

Fear thou not

Yadin Dudai

Mice lacking a certain neurotransmitter receptor have trouble forgetting scary experiences. This finding uncovers a fear-regulating feedback loop in the brain that might be at work in humans, too.

"Show me a man," said the Roman writer Seneca, "who is not a slave; one is slave to lust, another to greed, another to ambition, and all men are slaves to fear." There are few who would seriously challenge this 2,000-year-old conclusion, and fear of fear is probably one of the major motivations for studying emotions in general. Until quite recently, however, it was considered unfashionable for respectable brain scientists to investigate the molecular and cellular bases of the emotions. This has now changed, and we have ample information about the brain circuits that encode fear[1]. Writing last month in *Cell*, Shumyatsky and colleagues[2] have added important details to the emerging picture. Besides exposing tricks used by the brain to manage fear, the new findings might, in the long run, pave the way to improved treatments for pathological fear responses such as post-traumatic stress disorder.

Study of the cellular and molecular bases of fear requires a model system in laboratory animals. The most popular model is classical (alias pavlovian) 'fear conditioning'. To understand how this works, it helps to recall how Pavlov trained his dogs in his St Petersburg lab a century ago. In a typical experiment, a dog was presented with a sound, and

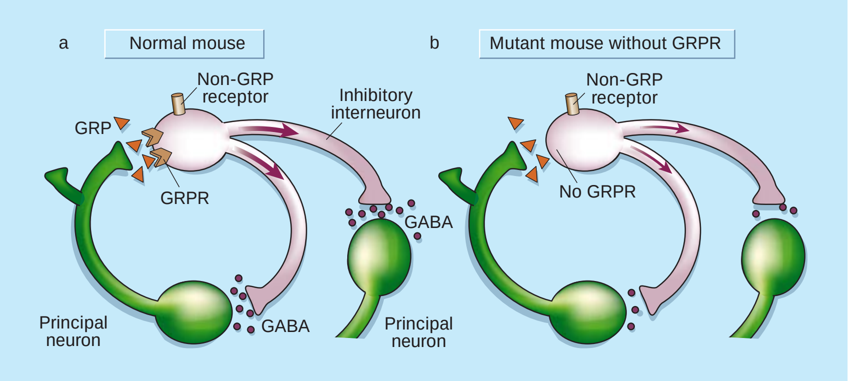

Figure 1 **Neuronal circuits and frightened mice. Shumyatsky *et al.*[2] have proposed the following model for a negative-feedback loop that modulates the activity of the principal neurons in the brain's lateral amygdala, thereby controlling memories of fearful stimuli.** a, **In normal mice, the principal neurons process and transmit information relevant to the formation of fear-associated memories. On activation, these neurons release (among other neurotransmitters) the peptide GRP onto inhibitory interneurons that carry the GRP receptor (GRPR). These interneurons release the inhibitory transmitter GABA onto the principal neurons. Activation of the GRPR stimulates the interneurons to release more GABA, increasing inhibition of the principal neurons.** b, **In mice in which the GRPR is knocked out, the inhibitory interneurons are insensitive to GRP, the feedback loop is severed, and the principal neurons are not properly inhibited. The mice form an abnormally strong and persistent fear memory. The innate level of anxiety and memories of non-fearful events are not affected. (Modified from ref. 2.)**

immediately afterwards with meat, which evoked salivation. In the language of psychology, the sound is the conditioned stimulus, the meat the unconditioned stimulus, and salivation in response to meat is the unconditioned response. With time, the dog learned that the sound predicted food, and salivated when presented with the sound alone (the conditioned response). Now, let's substitute the dog with a mouse (or rat), keep the sound, but replace the food with an electric shock to the foot. The result is that the mouse learns to fear the sound. Fear has many manifestations, one of which — freezing of movement — is commonly used as the conditioned response in lab animals.

Part of the neuronal circuitry that subserves fear conditioning is found in the amygdala, a collection of neural structures in the temporal lobe of the brain that controls many aspects of emotional and social behaviour. According to a generally accepted model, information about the conditioned and unconditioned stimuli becomes associated in the lateral nucleus of the amygdala, and output from the amygdala controls the expression of fear (reviewed in ref. 3). Although its exact role is still uncertain[4], the amygdala is known to be essential for the formation of memory of fearful experiences. Furthermore, in keeping with the conceptual framework that underlies contemporary neurobiology, it is believed that 'fear' in the amygdala to previously innocent stimuli is caused by experience-induced changes in its synapses (the connections between nerve cells).

The molecular basis of fear conditioning is one of the hottest topics in memory research[5–7], and Shumyatsky *et al.*[2] have now tackled certain aspects of it. First, they compared gene expression in different brain areas in mice. This led them to identify a gene coding for a neurotransmitter (a molecule that transmits information between neurons) called gastrin-releasing peptide (GRP), which they found to be preferentially expressed in the principal type of nerve cells in the lateral amygdala and in some interconnected brain areas. The authors then searched for cells that contained the GRP receptor (GRPR) and that could therefore react to GRP. They found the receptor in a subpopulation of amygdalar interneurons — another type of nerve cell — that release the neurotransmitter γ-aminobutyric acid (GABA).

GABA inhibits nerve-cell activity, and Shumyatsky *et al.* found that GRP causes the GRPR-expressing population of interneurons to release more GABA, augmenting their inhibition of the principal cells (Fig. 1a). This effect was abolished in mutant mice in which the GRPR gene was knocked out (Fig. 1b). Moreover, these mutants also displayed enhanced long-term potentiation (LTP) in the neuronal pathway linking the cortex — which perceives and processes fear-associated stimuli, such as the sound in fear conditioning — and the amygdala. LTP is an enhancement of synaptic transmission that persists after repetitive stimulation of a particular neuronal pathway, and it is a major model for learning-related changes in the mammalian brain. Moreover, LTP has been shown to contribute to fear learning *in vivo*[8]. So, this all adds up: an absence of GRPR impairs the inhibition of the principal amygdalar cells by interneurons, and this allows synapses between the neurons of the cortex and amygdala to become more susceptible to LTP.

Together, the data indicate that the lateral amygdala contains a loop that involves the principal neurons and the GRPR-containing inhibitory interneurons. These interneurons regulate the fear-related information that the principal cells process. When the principal neurons fire, they release, among other molecules, GRP, which interacts with GRPR on the interneurons and enhances their inhibition of the principal neurons. So this is a negative-feedback loop.

How is this relevant to behaviour? Shumyatsky *et al.* found that the GRPR-deficient mice displayed a greater and more persistent long-term memory of fear. These mice were not, however, generally anxious, nor did they have a stronger memory of non-fearful events. In other words, the GRP-mediated negative-feedback loop in the amygdala seems to be involved specifically in registering emotionally traumatic experiences.

Several points are noteworthy. First, this work epitomizes the kind of multi-level approach that is essential for real progress in memory research. Second, Shumyatsky *et al.* have dissociated two tiers in a mechanism that regulates the balance between excitation and inhibition in the amygdala. One tier, involving the basal activity of the inhibitory neurotransmitter GABA, controls the innate level of anxiety; the GRPR mutants might have lived happily for ever in a world without painful surprises, because normal basal levels of GABA are released from the inhibitory interneurons in their amygdalas.

The other tier involves the fine-tuning by experience of this balance between excitation and inhibition. This tier constrains the reaction of organisms to emotional trauma. Here GRP is important, and so mutants with a defective GRP-mediated negative-feedback loop overreact to fearful life experiences and have trouble forgetting them, presumably because they lack the mechanism that, in normal mice, quenches fear-induced overactivation of the principal amygdalar neurons. A final point is that only a subpopulation of amygdalar interneurons responds to GRP; other amygdalar circuits, using different neurotransmitters, might fine-tune other emotions.

It will be interesting to see whether these findings translate to humans. Might, for instance, experience-dependent alterations in the GRP-mediated feedback loop contribute to post-traumatic stress disorder following devastating experiences such as rape or a terrorist attack? Might defects in this neuronal system be identified in people who are particularly susceptible to post-traumatic stress disorder? And do some of us overexpress GRP or GRPR, ultimately rendering us less easily frightened than others because we forget scary experiences more quickly? Surely, we are all anxious to know the answers to these questions. But even before we do, the GRP system is likely to become a focus for research into new, selective, anxiety-relieving drugs. ■

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Thermal physics

Heat in one dimension

Roberto Livi and Stefano Lepri

Heat is transferred along a temperature gradient, from hot to cold, at a rate determined by the thermal conductivity of the material. But is the situation so straightforward in fewer than three dimensions?

Many phenomena in nature occur as the result of some kind of imbalance. For instance, an electric current flows when there is a difference in electric potential along a conductor (such as when an electric field is applied), and heat is transported when there is a temperature gradient between two boundaries of a material. Despite their ubiquity in everyday life, many aspects of such phenomena are still the subject of debate among theoretical physicists. One central issue is the role of spatial constraints, caused by the dimensionality of a system: the response of a system to external forces is intimately related to statistical fluctuations within it, and these, in turn, depend strongly on whether the system is one-, two- or three-dimensional. What happens to energy or charge transport in systems that are effectively one-dimensional, such as a nanowire or a DNA molecule? Onuttom Narayan and Sriram Ramaswamy[1] give their answer in *Physical Review Letters*.

Because of the variety and complexity of specific interactions, simplified microscopic models are an invaluable tool for the study of transport mechanisms in reduced dimensions (Fig. 1). An example is the old problem of heat conduction. Our own simulations[2,3] using models of classical low-dimensional fluids and crystals show that the thermal conductivity should increase with the system size. In other words, the larger the system, the more efficiently heat is transported (assuming that the density of the material and the temperature gradient are fixed) — in physical terms, the mean free path of the 'heat carriers' increases with the length of the sample.

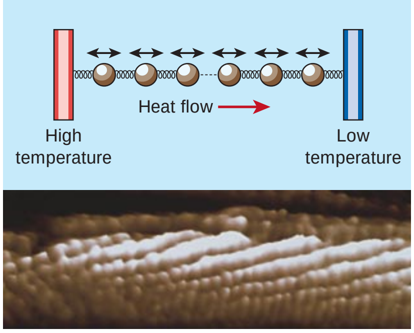

Figure 1 **Simple models and real materials. Modelling anomalous heat conduction in one-dimensional systems of interacting particles — such as a chain of oscillating particles that connect two reservoirs at different temperatures (above) — is relevant for understanding heat transport in single-walled carbon nanotubes (below).**

SPL

Narayan and Ramaswamy[1] are now able to justify this unusual behaviour. They considered a normal fluid, in which the only quantities that vary in time and space are mass, momentum and energy density. They show analytically that the usual concept of thermal conductivity is not well defined for a system of fewer than three dimensions — confirming that space dimensionality is crucial in anomalous transport properties. More specifically, they have estimated that the thermal conductivity diverges as the length of a one-dimensional system increases, following a power law with exponent 1/3; for a two-dimensional system, the divergence is much weaker and logarithmic. But such anomalous behaviour disappears in three dimensions.

Transport anomalies such as this have been found in many microscopic models, including one-dimensional crystals. Although it may seem strange to consider a one-dimensional crystal as a fluid, it is nonetheless well known that mechanical vibrations in a crystal structure can be described by hydrodynamic equations similar to those used in a fluid, as interacting phonons in a crystal behave similarly to particles in a fluid. And as Narayan and Ramaswamy[1] discuss, it is reasonable to expect that the same equations should also be applicable to models of low-dimensional lattices.

For the case of particular lattices of particles known as Fermi–Pasta–Ulam chains, we have performed extensive computer simulations[3] that also indicate a power-law divergence for the thermal conductivity in one-dimensional systems. But our finding for the index of the power law (a value greater than 0.36) is not fully in agreement with Narayan and Ramaswamy's prediction of 1/3. These authors suggest that the discrepancy might arise because, in the one-dimensional case, a fluid and a lattice shouldn't be considered to be exactly equivalent, at least for the intermediate sizes and timescales currently accessible in simulations. In this respect, there are open questions: can the anomalous behaviour actually be described by universal scaling laws, and to what extent does it depend on the nature of the microscopic interactions?

The conceptual challenge is not the only reason for studying energy transport in spatially constrained systems — there is also a variety of real systems in which these anomalies are important. Anisotropic crystals, magnetic chains, polymers and semiconductor films or wires are all examples of systems in which modern experimental techniques can probe the transport properties directly. Single-walled nanotubes (Fig. 1) are known through experiment to have an unusually high thermal conductivity, which is attributed mainly to quasi-one-dimensional lattice vibrations[4,5], and it is reasonable to expect that the scaling laws derived for simple models should apply to nanotubes as well[6]. Although, so far, an experimental test is lacking, molecular-dynamics simulations that use realistic energy potentials for the carbon atoms support this idea[7]. If the thermal conductivity did increase with nanotube length in a well-defined way, this would be a very promising feature to use in technological applications, such as the design of components that dissipate heat efficiently in nanocircuits.

In building models of energy-transport processes, the aim is to single out generic physical features, although this might sometimes be at the price of drastic simplifications. Hopefully, in the end the results will go beyond pure academic interest and suggest new ideas for technological applications — perhaps the reader is astonished that so many interesting and innovative ideas are still emerging from classical mechanics. ■

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