

theory hangs on the answer to the question: "What have the Gaiaans ever given us?". One response, raised in the summing up (L. Kump, Penn State Univ.), is that an appreciation of Gaia theory has shifted thinking in Earth systems away from cataloguing the fluxes and pools of the Earth's major elements, and towards identifying control systems and feedbacks. Moreover, we have a reminder that there is no harm in taking ideas that were once regarded sceptically and following them through with rigorous

analysis. From these considerations alone, it seems that the general scientific environment has now become hospitable enough for the Gaia hypothesis to last into the future. But how it might evolve is anyone's guess. ■

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Neurobiology

## The shaky trace

Yadin Dudai

Penelope would have been sad indeed had she realized that each time she was reminded of her beloved Odysseus — away from home for so many years after the Trojan war<sup>1</sup> — she could entirely lose her precious memory of him. Fortunately this was also unknown to her pushy suitors. But now Nader and colleagues, writing on page 722 of this issue<sup>2</sup>, have made it public. Recollection, they claim, is a dangerous matter: whenever we bring a memory to mind, it may turn shaky and slip into oblivion.

Most memories, like humans and wines, do not mature instantly. Instead they are gradually stabilized in a process referred to as consolidation<sup>3,4</sup>. Newly formed memory traces are sensitive to a variety of brain injuries and drugs, but after they have been consolidated they become more resistant to these treatments. Consolidation takes place at many levels of organization and complexity in the brain, and its overall kinetics depends on the type of memory involved. We know most about what happens in individual nerve cells and synapses — the points of communication between neurons — once they have been recruited to consolidate a memory.

The current textbook version, in a nutshell, goes like this. Training modifies proteins at synapses in the neuronal circuit that acquires the new memory. This alters synaptic efficacy and thus the encoding of information in that circuit. But protein molecules survive only for periods of minutes to weeks, whereas many memories are destined to live longer. It seems that at least part of the immunity of memory to this molecular turnover is achieved by training-induced modulation of gene expression in the modified neurons. The new gene products promote long-lasting remodelling of the activated synapses, in a process that involves crosstalk between the synapses and neuronal cell bodies<sup>5</sup>. It takes a few hours for the new pattern of gene expression and the synaptic change to be consolidated. During this time,

the process can be halted by inhibitors of protein synthesis<sup>5–7</sup>.

This textbook version might tempt one to believe that, for every memorized item, consolidation starts and ends just once. But this view would be naive. Experimental psychologists told us long ago that memory traces are reconstructed with use, and that retrieving a memory involves mingling the representations of the past with the percepts of the present<sup>8</sup>. The study by Nader *et al.*<sup>2</sup> echoes earlier reports that a consolidated memory can apparently be induced to vanish, provided that the memory is activated shortly before the use of the treatment leading to amnesia<sup>9,10</sup>. The problem with these early studies was that, because the treatments were applied to the whole brain or even the whole body, and because little was known about the relevant neuronal circuits, the researchers could not target cellular mechanisms in identified memory traces. This has now changed.

Nader *et al.* took advantage of 'auditory fear conditioning' in rats. This works as follows. The rat hears a tone (the conditioned stimulus) in conjunction with a mild foot-shock (the unconditioned stimulus). The electric shock elicits fear (an unconditioned response). After one training session, the tone elicits fear responses, such as freezing, even in the absence of shock (a conditioned response). For readers who are not well versed in the emotional life of rats but do recall the story of Pavlov and his salivating dogs, suffice it to note that the situations are basically similar: both the dogs in Petrograd and the rats in Manhattan had to learn to associate conditioned and unconditioned stimuli. The protocol is therefore aptly dubbed 'pavlovian fear conditioning'. The neuronal circuit underlying pavlovian fear conditioning includes the lateral and basal nuclei of the amygdala. Inhibiting protein synthesis in this brain region immediately after fear conditioning, by infusing the antibiotic anisomycin into this region, blocks long-term fear memory

(that existing more than 24 hours after the training), but not short-term memory<sup>2</sup>.

Knowing all this, Nader *et al.* trained rats in pavlovian fear conditioning, and tested them 24 hours later with the conditioned stimulus but without the unconditioned stimulus (test 1). The rats froze at the sound of the tone. At this point, when the long-term memory trace was expected to be already insensitive to anisomycin, Nader *et al.* injected the antibiotic into the amygdala. A day later, the authors tested the rats again with just the conditioned stimulus (test 2). Surprisingly, these rats showed a marked decrease in the time spent freezing in response to the tone. The same results were obtained even if test 1 took place 14 days after training, making it even more unlikely that the inhibition of protein synthesis in test 1 impaired a late phase of consolidation initiated by the original training. Omitting the conditioned stimulus before administering anisomycin in test 1 left memory intact. So the memory probably had to be retrieved for anisomycin to have its effect. The anisomycin was effective only if administered within a few hours after memory reactivation.

So it seems that fear-associated memories become temporarily labile on retrieval. Why should the brain invest so much energy in the original consolidation and then risk losing the trace by interference each time it is used? One can come up with teleological explanations — for example, that the brain prefers plasticity at the expense of stability — or mechanistic ones, suggesting in-built constraints on the synaptic machinery. But there is still much to do before we can jump to any sweeping conclusions about the cellular biology of memory retrieval. Some unanswered questions relate specifically to this experiment. Did tests 1 and 2 indeed tap the same memory trace? Did anisomycin abolish the original trace, or merely leave it dormant, waiting to be exposed by some smart behavioural protocol? Which cellular mechanisms are perturbed by anisomycin after retrieval, and are they identical to those that produce the original consolidation?

More generally, might these results apply to different types of memory? Previous studies hinted that pavlovian fear conditioning may not be unique in being shaky on retrieval<sup>9,10</sup>. But even if just a few types of memory must reconsolidate after use, the implications of the results of Nader *et al.*<sup>2</sup> are remarkable. Consider, for example, the prospect of intentionally recalling the memory of a traumatic experience and then selectively erasing it. What such a possibility would mean for psychoanalysts on the one hand, and poets on the other, is quite a different matter. ■

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Organic materials

# From insulator to superconductor

Philip Phillips

The discovery in the late 1970s that certain types of polymeric material<sup>1</sup> can conduct electricity almost as efficiently as copper wire paved the way for light-emitting diodes, electrical sensors and even rechargeable batteries made entirely from plastics. This success sparked general interest in electronic devices made from cheap organic materials, such as organic superconductors<sup>2</sup>. In a superconductor, electrons bind together to form Cooper pairs that carry current without resistance at sufficiently low temperatures. On page 702 of this issue<sup>3</sup>, Batlogg and his colleagues describe how to make superconducting transistors from anthracene, tetracene and pentacene. Under normal conditions, these simple organic materials are insulators, but they can be converted into superconductors simply by injecting them with charge and lowering the temperature.

The organic crystals studied by Batlogg and colleagues are composed of three (anthracene) to five (pentacene) linked rings of carbon atoms. As part of a transistor they can conduct electricity, and at low temperatures of 2–4 K their electrical resistance drops to zero. This superconducting behaviour is destroyed by an applied magnetic field. Zero resistance and expulsion of magnetic fields are intrinsic features of a true superconducting state. But given the high superconducting transition temperatures ( $T_c = 135$  K) that have been observed in copper-oxide compounds, why should we care about a relatively low  $T_c$  in an organic transistor? The answer is simple — these materials are far from being ordinary superconductors and offer a fertile playground for studying the fundamental properties of correlated electrons.

Batlogg and colleagues build their organic superconductors from highly pure single crystals of polyacenes coated with an insulator, typically aluminium oxide. By fixing a gate electrode to the oxide layer and placing source and drain electrodes on the organic crystal, they create a field-effect transistor (see Fig. 1 on page 702). Applying a voltage to the gate electrode triggers a flow of charge between the other two electrodes. Such a device is electrically identical to those made from semiconductors, such as silicon (Si) and

gallium arsenide (GaAs). What is different about the organic devices is that they become superconducting at high charge densities. Superconducting materials have been created from insulators before by doping them with oxygen, as in the case of the copper oxides; but this new type of ‘charge doping’ greatly broadens the range of materials that can be converted into superconductors.

Superconductivity is generally associated with a bulk material. But in these experiments, electrons cannot penetrate the insulator. As a result, they are confined to move within the thin two-dimensional interface between the organic crystal and the oxide. This is significant because, in the past 20 years, the physics of two-dimensional electron gases has dominated solid-state research, resulting in Nobel prizes in 1985 and 1998. Exotic phases, such as those found in copper-oxide superconductors or in a highly correlated electron liquid state with fractionally charged excitations<sup>4</sup>, are the main reasons why the physics of correlated two-dimensional electrons is such an important problem. Many of these exotic states can now be studied in an organic field-effect transistor — indeed, Batlogg’s group has already observed the quantum Hall effect in pentacene<sup>5</sup>.

As with any discovery of superconductivity, the physical mechanism behind the electron pairing is the key issue. It is worth noting that no chemically doped polyacene has ever been observed to superconduct. In this respect, the observation of superconductivity in a fullerene ( $C_{60}$  molecule) transistor<sup>6</sup> is quite different from that in the polyacenes, because  $C_{60}$  doped with alkali metals superconducts. Furthermore, it is thought<sup>7</sup> that doped  $C_{60}$  follows the standard picture of superconductivity in which tiny lattice vibrations (or phonons) provide the glue that binds electrons in pairs. The strength of this glue can be inferred from the electron–phonon coupling constant<sup>8</sup>. For a series of organic compounds, including the polyacenes and  $C_{60}$ , the electron–phonon coupling constant falls off inversely with the number of  $\pi$ -electrons associated with the carbon rings (Fig. 1).

On the basis of this trend, one expects anthracene to have the highest superconducting transition temperature,  $T_c$ , within the polyacene series studied by Batlogg and co-workers. Indeed, this is what they find. But one also expects doped  $C_{60}$  to have the lowest, whereas it has a much higher  $T_c$  of 33 K. The explanation may lie in differences in their density of electronic states. It is the product of the density of states and the electron–phonon coupling constant that determines, to a large extent, the value of  $T_c$ . But an independent measure of the density of states is difficult to achieve experimentally unless thermodynamic measurements are made. Such measurements would be particularly difficult in the polyacene crystals because the electron gas is sandwiched between two insulators.

An experiment that could help determine the mechanism of pairing in the polyacenes (and that is now possible) would be to probe the properties of a pentacene transistor at low temperatures and low electron densities.

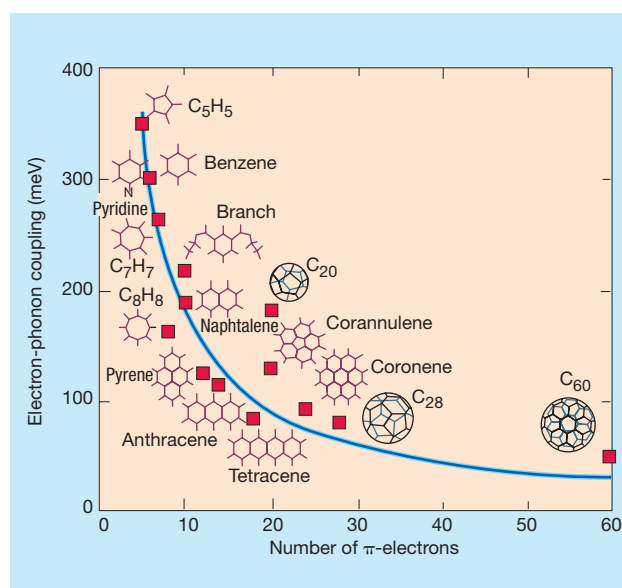


Figure 1 What lies behind the superconductivity of organic materials, such as polyacenes (anthracene) and fullerenes ( $C_{60}$ )? A clue might be provided by the electron–phonon coupling constant for a series of organic semiconductors is shown as a function of the number of  $\pi$ -electrons associated with their carbon rings. (Redrawn from ref. 8.)