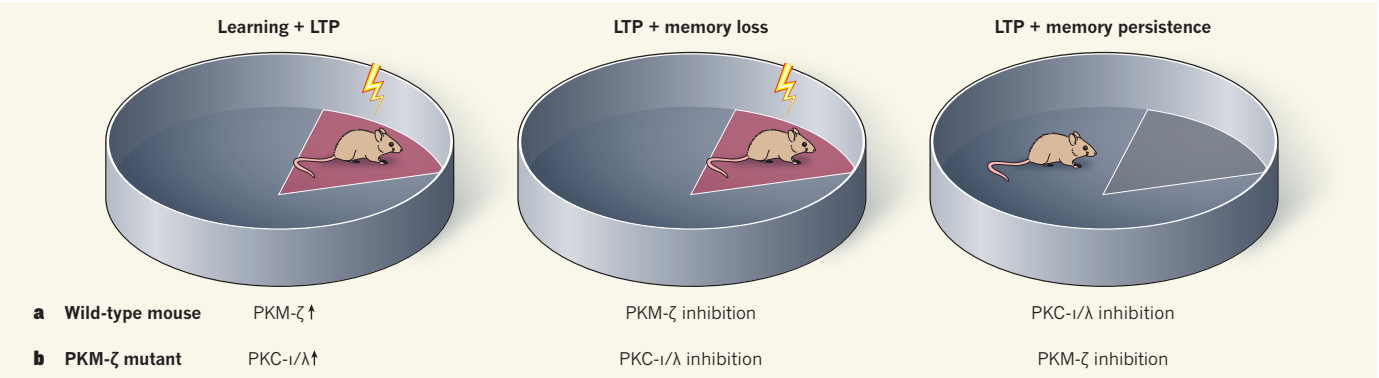

Figure 1 | Memory loss modulated. In place-avoidance tests, mice learn that they will receive a foot shock if they move over a certain part of a rotating test arena. During this learning, the synaptic connections between neurons are strengthened in a process called long-term potentiation (LTP), which is required for memory formation. Tsokas *et al.*[4] investigated how two atypical isoforms of the enzyme protein kinase C — PKM-ζ and PKC-ι/λ — regulate memory maintenance following LTP induction. **a**, In wild-type mice, levels of PKM-ζ rise following learning. Inhibition of PKM-ζ in these mice causes loss of LTP and hence loss of memory, so the mice forget how to avoid a shock. By contrast, inhibition of PKC-ι/λ has no effect on memory of the learned activity. **b**, In mice that lack the gene encoding PKM-ζ, PKC-ι/λ is elevated following LTP induction. Inhibition of PKC-ι/λ causes LTP and memory loss, whereas PKM-ζ inhibition has no effect. Thus PKM-ζ is the main substrate for memory maintenance in normal conditions, but PKC-ι/λ can compensate in its absence.

LTP in slices from normal mice. ZIP treatment reversed the effects of either protein injection, hinting that PKC-ι/λ might be the mystery molecule that compensates for loss of PKM-ζ.

To test this idea directly, Tsokas and colleagues inhibited either PKM-ζ or PKC-ι/λ and examined LTP in hippocampal slices (Fig. 1). In slices from control mice, inhibiting PKM-ζ blocked LTP, but PKC-ι/λ inhibition had no effect. By contrast, in PKM-ζ-deficient mice, inhibiting PKC-ι/λ blocked LTP, but PKM-ζ inhibition was ineffective. The same pattern emerged when the authors examined the effects of PKC-ι/λ and PKM-ζ inhibition on memory in control and PKM-ζ-deficient mice.

Do these latest results restore the position of PKM-ζ as the leading memory molecule? The allure of the PKM-ζ theory is the idea that a single molecule is responsible for maintaining LTP and memories. The current findings are not inconsistent with this view. However, in their experiments, Tsokas *et al.* inhibited PKM-ζ in normal mice before (rather than after) LTP and memory induction. This means that they cannot directly evaluate the enzyme's role in the persistence of LTP and memory.

The PKM-ζ saga serves as a cautionary tale about the specificity of the tools that we use to examine brain function and establish causality. The controversy exposed the bluntness of ZIP as a tool for probing PKM-ζ function because it clearly affects other molecules and may even lead to neuronal silencing[10]. Equally, seemingly more specific interventions, such as genetic deletion of PKM-ζ, produced a cascade of unintended compensatory changes, which clouded interpretations and masked predicted outcomes. This limitation is not restricted to genetic mutations, but extends to any intervention that perturbs brain function (such as optogenetic or chemogenetic strategies in which genetically introduced proteins can be activated and inhibited in response to light or drugs).

As the PKM-ζ debate rumbles on, there is a broader mystery to consider. Molecular neuroscientists such as Tsokas and colleagues present a static view of the engram, in which patterns of synaptic changes that are initiated during memory encoding are maintained over the lifetime of the memory. By contrast, systems neuroscientists present a more dynamic picture, emphasizing memory maintenance in the midst of broad changes in the synapses[11] and even the neurons[12] that correspond to the engram. A full account of memory persistence needs to merge these molecular and systems perspectives, allowing the twain to meet. ■

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This article was published online on 29 June 2016.

CHEMICAL PHYSICS

Quantum control of light-induced reactions

An investigation of how ultracold molecules are broken apart by light reveals surprising, previously unobserved quantum effects. The work opens up avenues of research in quantum optics. SEE LETTER P.122

DAVID W. CHANDLER

The rupture of molecular bonds by the absorption of light drives chemistry in the atmosphere, causes DNA damage and the associated repair response, and provides a superb tool to study how molecules absorb light and then distribute and dispose of its energy. On page 122, McDonald *et al.*[1] report their study of the light-induced break-up (photodissociation) of ultracold strontium molecules, Sr_2. Their work provides insight into how molecules behave in the quantum regime of ultralow-energy dynamics that occurs just above energy thresholds for photodissociation.

Early photodissociation studies focused on

the energetics[2] of the products formed from diatomic molecules, and of the products' angular distribution[3] — the distribution of angles at which they recoil relative to the direction of polarization (the polarization axis) of the light that excited them. If the energy of the photon absorbed by the diatomic molecule and the velocities of the resulting atomic fragments were known, then the bond energy of the molecule could be directly determined. The accuracy of these determinations depended on how cold the molecule was initially, and on how accurately one could measure the velocities of the products.

In the early experiments[4], diatomic molecules were irradiated with laser light, and if the fragments were found to fly predominantly parallel to the laser polarization axis, then the transition dipole moment responsible for the light absorption was said to be parallel; similarly, perpendicular transitions were named after the associated perpendicular recoil. The transition dipole moment describes coupling between the two electronic states responsible for light absorption, and this classification was helpful in understanding its nature. For polyatomic molecules, the transition dipole moment does not have to align with a particular molecular axis, and many factors affect the measured angular distribution of the fragments. Measurements of the velocities of fragments provide information about the dynamics of the energy deposited within molecules as it evolves into the kinetic energy of the fragments.

Hundreds of photodissociation studies have been performed because of the fundamental information that can be obtained. With the advent of laser-based imaging techniques[5–8] in the late 1980s, it became possible to measure velocities at high resolution (approximately a few metres per second) for particular electronic states of the products, by projecting the ionized products onto position-sensitive ion detectors. However, these experiments typically used pulsed-dye lasers (which produce light at a low frequency resolution of about 3,000 megahertz) to dissociate molecules and detect the products. This precludes experiments such as those performed by McDonald and colleagues, in which molecules are dissociated by photons that have a much higher, 1 MHz frequency resolution and energies just above the dissociation threshold of the molecule (that is, at light frequencies between 5 and 400 MHz greater than the dissociation-threshold frequency).

Moreover, these experiments typically used supersonic molecular beams as a source of cool molecules. When a high-pressure gas is expanded into a vacuum to form a molecular beam, the flow is directed forward supersonically at the expense of the kinetic energy associated with the other directions of flight and with the gas's internal degrees of freedom (the rotational and vibrational motion of its molecules). This allows molecules to be cooled to temperatures of a few kelvin even though they fly at close to velocities of 1,000 m s^{-1}, with a spread of about 50 m s^{-1}. McDonald and co-workers, however, wanted to study photodissociation fragments moving at only about 1 m s^{-1} (extremely slowly for a molecule, and correlating with a temperature of tens of millikelvin). To see such slow fragments, the authors held their molecules in a stationary laser trap, photodissociated them using a light pulse and then imaged the fragments after they had flown for about a hundred microseconds.

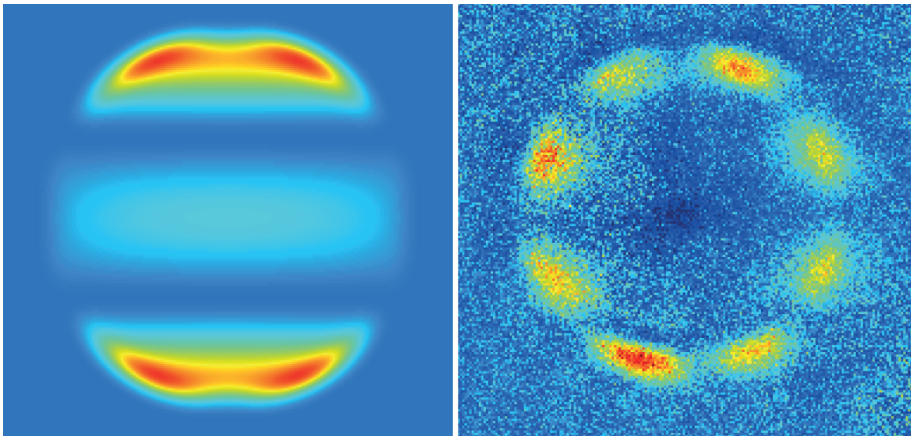

Figure 1 | Quantum effects in photodissociation. McDonald *et al.*[1] studied the light-induced fragmentation (photodissociation) of diatomic strontium molecules, Sr_2, and observed surprising angular distributions of the resulting products. The left-hand panel shows a two-dimensional representation of the angular distribution of fragments obtained from Sr_2 in a particular rotational quantum state, as predicted by quasiclassical theory; hot colours indicate higher distributions of fragments. The right-hand panel indicates the experimentally observed pattern, which can be explained only by using a full quantum-mechanical description of photodissociation.

Molecules can interact with light through either the light's oscillating electric field (which causes electric dipole transitions) or its oscillating magnetic field (magnetic dipole transitions). For most covalently bound molecules, the light intensity required to produce electric dipole transitions is a million times less than that required for magnetic dipole transitions. McDonald *et al.* are the first to have excited a pure magnetic transition and observed the fragments. This was possible because the Sr_2 molecules in this study are formed in the highest vibrational energy levels of the molecule's ground state, and therefore have a very long bond length, which increases the magnetic transition dipole moment by approximately 1,000-fold[9].

Another groundbreaking feature of McDonald and colleagues' work is that the Sr_2 molecules were prepared in a single rotational and vibrational quantum state by the laser-induced association of ultracold atoms, in the presence of an oriented magnetic field. Each state represents the projection (M) of a molecule's angular momentum vector (J) onto a quantization axis (in this case, the quantization axis aligns with the magnetic field). Several M states exist for each J value, and in the absence of a magnetic field they have the same energy (they are said to be degenerate); the number of M states is defined by the formula $2J+1$. When J is zero, it has no magnitude and no alignment in space. In a magnetic field, the M states do not have the same energy, because rotating electrons create a magnetic field that can be either aligned or counteraligned with the external magnetic-field quantization axis.

The authors' experiments started from a single (J,M) quantum state formed in the laser-association process. All of the quantum states reached during photodissociation were dictated by the starting state, and by the laser frequency and polarization relative to the magnetic field's axis. When the researchers obtained a single excited quantum state, they observed fragments recoiling predominantly parallel or perpendicular to the laser polarization. But if several degenerate quantum states were excited and interfered with each other, then the observed velocity distribution deviated spectacularly from purely parallel or perpendicular. These unexpected and previously unobserved angular distributions can be described only by a full quantum-mechanical treatment of the light-absorption process (Fig. 1).

At present, this sort of experiment is limited to a few diatomic molecules — some of which, like Sr_2, are not covalently bound — that can be generated by cold-atom techniques. However, there is much to be learnt from these studies, and as scientists learn to cool and trap a larger array of covalently bound molecules, the techniques developed and knowledge gained will provide the foundation for future research — for example, in polyatomic molecules. The photo-physics of polyatomic molecules is more complex than that of diatomic molecules, because multiple mechanisms couple their electronic states to each other, and several fragmentation pathways are possible. In the meantime, I personally found this article a joy to absorb. ■

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CONSERVATION

The rainforest's 'do not disturb' signs

A study reveals that human-driven disturbances in previously undisturbed Amazon rainforest can cause biodiversity losses as severe as those of deforestation. Urgent policy interventions are needed to preserve forest quality. SEE LETTER P.144

DAVID P. EDWARDS

As we enter the Anthropocene, a proposed geological epoch shaped by human activity, mankind is driving a global biodiversity extinction crisis[1]. The conversion of forest to agricultural land is widely considered to be the leading cause of this crisis, especially in the hyperdiverse tropics[2], so avoiding deforestation is the predominant strategy for biodiversity conservation[3]. On page 144, Barlow *et al.*[4] present a landmark field study of Amazonian biodiversity in which they challenge the adequacy of this strategy by demonstrating the striking magnitude of several types of human-associated forest disturbance that are less immediately visible than deforestation.

Many studies have identified the negative effects on biodiversity of individual kinds of disturbance in tropical forests. These include the hunting of large animals[5], the selective logging of large, marketable trees[6], forest fires[7] and the creation of new edges to primary forests (those forests that have never been fully cleared) that, owing to deforestation, are buffeted by the hotter, drier and windier conditions found on adjacent farmland[8] (Fig. 1). However, by focusing on only one form of disturbance, such studies may have overlooked much greater conservation losses from the combined effects of forest disturbances.

Barlow and colleagues conducted biodiversity censuses across multiple landscapes and then developed a computational method for evaluating conservation losses (termed the 'conservation value deficit', a numerical value calculated by assessing biodiversity in disturbed primary forests relative to undisturbed ones). This enabled the authors to quantify the direct negative effects of deforestation and those resulting from the plethora of other types of forest disturbance.

The authors assembled an impressive data set collected across a large region of the Brazilian Amazon. They sampled 36 catchments (each 32–61 square kilometres in size) containing small rivers, spanning Belém and Tapajós, two major regions of endemism — areas that contain species that are found nowhere else. Each sample catchment varied in the degree of disturbance: 5 were entirely deforested, whereas the other 31 contained varying amounts of remnant forest, including undisturbed primary forests, and primary forests that had been disturbed by hunting, selective logging or fires, or isolated by surrounding farmland. Sampling the biodiversity across each catchment, Barlow and colleagues encountered a breathtaking total of 1,538 plant species, 460 bird species and 156 dung beetle species.

Their findings make for uncomfortable reading. Even catchments that retained 80% of their forest cover — the maximum that can be required of Amazonian estates under Brazil's Forest Code legislation — lost between 39% and 54% of their conservation value, and about half of this loss is due to disturbance within the remaining forest areas, rather than the losses from conversion to farmland. By extrapolating these disturbance-driven losses across the state of Pará, which represents 25% of the entire Brazilian Amazon, the authors found that conservation losses from disturbance are equivalent to the losses that would result from deforesting 92,000–139,000 km^2 of primary forest — an area roughly equivalent to the size of Greece.

They also found that species with higher conservation importance were more negatively affected by forest disturbance. Bird species that were restricted to small regions (with small global range sizes) fared worse than those with larger distributions, suggesting that forest disturbance is homogenizing biodiversity across regions[9]. Tree species with high wood density declined more than those with softer wood,

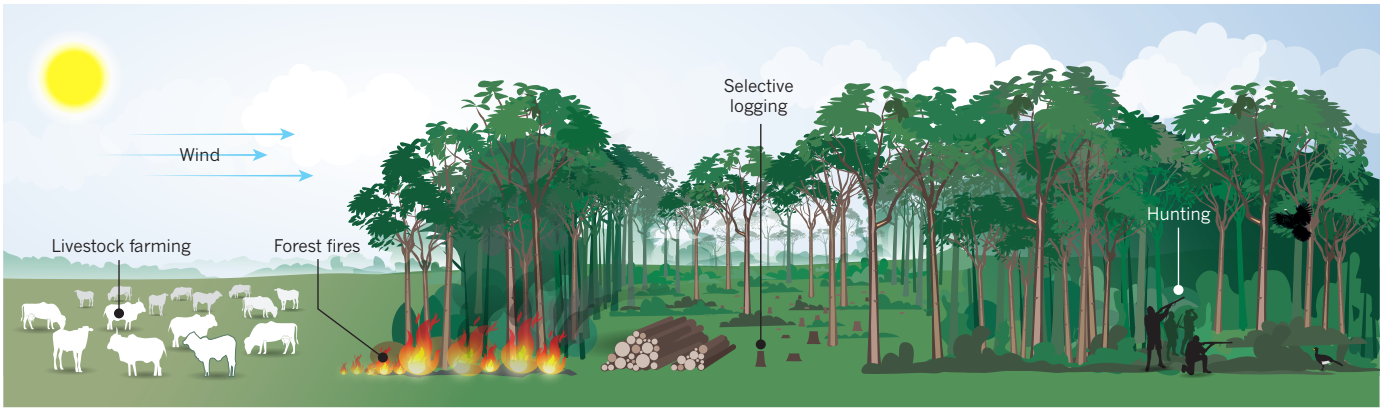

Figure 1 | Forest disturbance drives major conservation losses. Barlow *et al.*[4] report that the combined effects of various human-driven disturbances in the forests of the Brazilian Amazon can cause biodiversity losses on a scale similar to, or greater than, those caused by deforestation alone. Conversion to farmland can result in biodiversity loss and make forests more vulnerable to edge effects, such as the hot and windy conditions that can drive forest fires, which often ignite from farmland fires. Within the remaining rainforest, biodiversity can be affected by bushmeat hunting or selective logging.